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STUDIES ON OINTMENTS

VI. OINTMENTS CONTAINING CHRYSAROBIN

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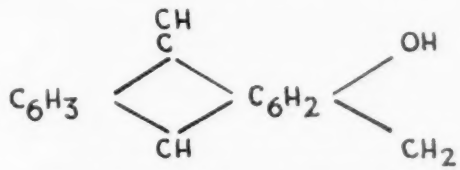
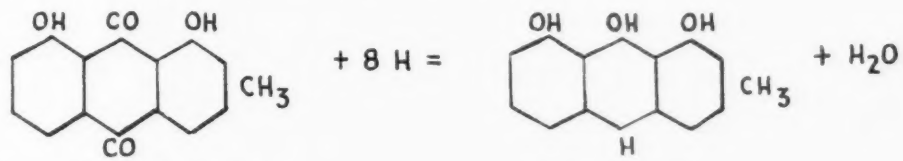
Chrysarobin was introduced into pharmacology by Balmanno Squire.[1] It was first found in cavities of the trunk of Andira araroba, a tree which grows in Brazil, in the Portuguese colony of Goa and elsewhere. The substance is crystalline, is tasteless and odorless, is slightly soluble in water, slightly soluble in alkalis (1 : 385) and partially soluble in fats and turns brown when exposed to the air. It belongs to the group of so-called "anthraglycosides" and has the following formula:



Senna, rhubarb, cascara, aloe and emodin are closely related drugs. Emodin, for instance, is a trioxymethylanthraquinone, $C_{15}H_{10}O_5$, while chrysarobin is formed from chrysophanic acid, $C_{15}H_{10}O_4$, in the following way:



dioxymethylanthraquinone, or chrysophanic acid

dioxymethylanthranol, or chrysarobin

An alkaline solution of chrysarobin exposed to the air turns into chrysophanic acid. Attfield [2] in 1875 analyzed chrysarobin, or "Goa powder" as it was called in those days, and found that its main constituent was chrysophanic acid, which he believed to be the therapeutic principle. The purified product was therefore called chrysophanic acid in England for many years thereafter. In contradiction to the belief of Attfield, the ordinary chrysarobin preparation contains only 2 per

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The third condensed part of a thesis submitted to the faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the Degree of Doctor of Philosophy in Dermatology and Syphilology.

1. Squire, B., cited by Perutz, A., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1930, vol. 5, pt. 1, p. 153.

2. Attfield, cited by Unna, P. G.: Cignolin als Heilmittel der Psoriasis, Dermat. Wchnschr. **62**:116, 1916.

cent chrysophanic acid according to Huerre [3] and is of no therapeutic value. Instead, it is responsible for the cutaneous irritation and should be removed from chrysarobin by treatment with potassium hydroxide.

Unna and Golodetz [4] were the first to study intensively the oxidation products of chrysarobin. Using a spectroscopic method, they demonstrated the formation of oxychrysarobin and chrysatoxin as well as chrysophanic acid as oxidation products of chrysarobin. Oxychrysarobin is characterized by an absorption band in the

Fig. 1.—Section showing the effect of 3 per cent chrysarobin in petrolatum after seven days. Note the partial keratolysis, parakeratosis and round cell infiltrations.

green and yellow and chrysarobin by a dark band in the red. Oxychrysarobin is formed by an alkali-free oxidation of chrysarobin by means of linoleic acid or lead oleate and forms spontaneously on the skin when alkali-free chrysarobin ointments are applied. If the oxidation is of short duration, chrysophanic acid is formed.

3. Huerre, M. R.: Acide chrysophanique et chrysarobin, Ann. de dermat. et syph. **10**: 364, 1929.

4. Unna, P. G., and Golodetz, L.: Zur Chemie der Haut: Die Oxydation des Chrysarobins auf der menschlichen Haut, Monatsh. f. prakt. Dermat. **51**:1, 1910.

Chrysatoxin forms when the oxidation is of longer duration. Oxychrysarobin is the main therapeutic principle according to Unna. As soon as chrysarobin is transferred into chrysophanic acid, it loses its therapeutic effect.

The oxidation of chrysarobin, therefore, occurs on the skin as soon as it comes into contact with oleic acid, which is formed by the sebaceous and sweat glands. Unna classified chrysarobin as a keratoplastic agent. Applied to the skin in higher concentrations, it causes a burning sensation, swelling, reddening and vesicle formation and eventually leads to exfoliation. It is a time-proved remedy for psoriasis, and von Sehlen [5] demonstrated as early as 1889 its value in the treatment of trychophytosis. It is not altogether harmless, since it causes severe conjunctivitis and

Fig. 2.—Section showing the effect of 5 per cent chrysarobin in zinc oxide paste after ten days. Note the exfoliation of the stratum corneum, parakeratosis, hemorrhage and round cell infiltration in the cutis.

even keratitis of the eye [6] when brought in contact with it; it also may lead to irritations of the kidneys. The brownish discoloration of the skin and clothing following its application is another unpleasant disadvantage.

EXPERIMENTAL STUDIES

Chrysarobin was incorporated into the following bases in strengths of 1, 3, 5 and 10 per cent: (1) petrolatum; (2) petrolatum and hydrous wool fat in equal

5. von Sehlen, D.: Ergebnisse der bakteriologischen Untersuchung bei der Chrysarobinbehandlung der Trichophytie, Monatsh. f. prakt. Dermat. **9**:547, 1889.

6. Igersheimer, J.: Ueber Schädigungen der Augen durch Chrysarobin, Klin. Monatsbl. f. Augenh. **1**:518, 1912.

parts; (3) a base consisting of 6 per cent of a group of esters of cholesterol (chiefly oxycholesterol) in an aliphatic hydrocarbon (petrolatum) base[7]; (4) a base consisting of fatty acid esters of diethanolamine mixed with petrolatum,[8] and two bases whose formulas are as follows: (5) stearyl alcohol[9] 10.0 Gm., liquid petrolatum 10 cc., water 10 cc. and light petrolatum 70 Gm.; (6) zinc oxide 7.5 Gm., talc 7.5 Gm. and enough petrolatum to make 30 Gm. The technic used was identical with that previously described.[10]

Hodara,[11] a pupil of Unna, was the only investigator to my knowledge who studied the histologic changes of the skin after the application of chrysarobin. He applied a 10 per cent chrysarobin "plaster" to the ear of a rabbit and performed biopsies after twenty-four hours. He also applied similar "plasters" to the skin of the forearm of 3 men and performed biopsies, the first after twenty-four hours,

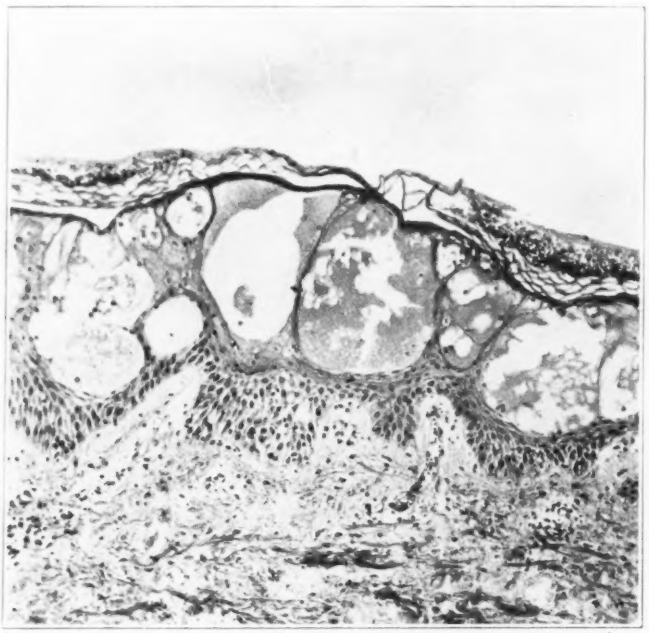

Fig. 3.—Section showing the effect of 10 per cent chrysarobin in the oxycholesterol-petrolatum ointment base after forty-eight hours. Note the vesicle formation, heavy intercellular and intracellular edema in the epidermis, and vascular dilatation in the stratum papillare.

the second after four days and the third after seven days. His conclusions were as follows: "Chrysarobin in low concentrations causes a homogenization and necrosis of the stratum granulosum and of a part of the stratum spinosum, as well as decided augmentation of the pigment in the stratum basale and in the necrotic

7. The preparation used was aquaphor, manufactured by the Duke Laboratories, Inc., Stamford, Conn.

8. The preparation used was hydrosorb, manufactured by the Abbott Laboratories, North Chicago, Ill.

9. The preparation used was lanette wax, SX, supplied by R. F. Revson Company, New York.

10. Strakosch, E. A.: Studies on Ointments: II. Ointments Containing Salicylic Acid, Arch. Dermat. & Syph. **47**:16 (Jan.) 1943.

11. Hodara, M.: Histologische Untersuchungen über die Wirkung des Chrysarobins, Monatsh. f. prakt. Dermat. **30**:53, 1900; **31**:261, 1900.

tissue, which eventually exfoliates in form of a scale. In higher concentrations it causes edema and a marked inflammation in the cutis, an intracellular and intercellular edema in the stratum spinosum leading to formation of vesicles. The latter dry up and become exfoliated, with their parakeratotic tops in form of a crust or scale which is loaded with yellow pigment. Underneath this necrotic stratum spinosum there are hypertrophy and mitotic proliferation of the younger prickle cells and follicle walls. There follows the formation of the new stratum

TABLE 1.—*Changes Observed After the Application of 1 and 3 per Cent Chrysarobin*

Base	Time, Days 1	2	3	7	10
Petrolatum	Slight homogenization of stratum granulosum	Homogenization of stratum granulosum; slight intercellular and intracellular edema; vascular dilatation	Edema of cutis; perivascular round cell infiltration	Parakeratosis and hyperkeratosis of stratum spinosum; mitosis in prickle cell layer	Beginning of vesicle formation; heavy perivascular round cell infiltration
Petrolatum-hydrous wool fat	No change	Slight intercellular and intracellular edema; vascular edema	Homogenization of stratum granulosum; perivascular round cell infiltration	Parakeratosis; hypertrophy of stratum spinosum	Beginning of vesicle formation; heavy perivascular round cell infiltration
Oxycholesterol-petrolatum Fatty acid esters of diethanolamine Stearyl alcohol Zinc oxide paste	No change	Slight intercellular and intracellular edema; vascular edema; slight homogenization of stratum granulosum	Homogenization of stratum granulosum; perivascular round cell infiltration	Parakeratosis; hypertrophy of stratum spinosum	Beginning of vesicle formation; heavy perivascular round cell infiltration

TABLE 2.—*Changes Observed After the Application of 5 per Cent Chrysarobin*

Base	Time, Days 1	2	3	7	10
Petrolatum	Homogenization of stratum granulosum; edema	Heavy intercellular and intracellular edema; vascular dilatation; round cell infiltration	Parakeratosis; hypertrophy of stratum spinosum; beginning of vesicle formation	Heavy parakeratosis; beginning of exfoliation of homogenized stratum granulosum; hemorrhage in cutis	Exfoliation of homogenized stratum granulosum; heavy round cell infiltration; edema of cutis
Petrolatum-hydrous wool fat Oxycholesterol-petrolatum Fatty acid esters of diethanolamine Stearyl alcohol Zinc oxide paste	Slight homogenization	Homogenization of stratum granulosum; intercellular and intracellular edema; vascular dilatation	Parakeratosis; severe inflammatory reactions	Heavy parakeratosis; beginning of vesicle formation; hypertrophy of stratum spinosum	Beginning of exfoliation of necrotic stratum granulosum; hemorrhage in cutis

granulosum and stratum spinosum, which are covered by a young stratum corneum containing little pigment. Similar changes were observed in the follicles." Vascular dilatation and perivascular lymphocytic infiltration as well as numerous mast cells may also be found.

These changes always occurred when ointments containing chrysarobin were applied to the skin. The intensity of the process and the time necessary to produce the changes varied according to the concentration of chrysarobin and the ointment base in which it was applied. The results of these experiments are presented in tables 1 and 2. The results observed with 10 per cent chrysarobin in all bases

used, with the exception of the zinc oxide paste, after forty-eight and seventy-two hour applications were like those observed with a 5 per cent concentration after seven days. The time required to obtain equal reaction was one to two days longer when zinc oxide paste was used as a base.

COMMENT

Analysis of these experimental results brings out three points of interest and of some practical value. First, equal reactions were obtained from a 1 and a 3 per cent concentration of chrysarobin, and although a 5 per cent concentration gave stronger reactions after corresponding times of applications, the differences were only slight. Thus, for all practical purposes there is no great difference between a 1 and a 5 per cent concentration. Secondly, the reactions were always more severe when petrolatum was used as a base. Finally, when chrysarobin was incorporated into zinc oxide paste its therapeutic action was not diminished as compared with the effects when other emulsion bases were employed. This is contrary to the observations made when salicylic acid,[10] sulfur [12] or resorcinol [13] was incorporated into zinc oxide paste. With these bases the concentration of the drug as well as the time of application had to be considerably increased to obtain reactions equal to those obtained when emulsion bases were used.

This study confirms in its major points the clinical observations of Siemens,[14] who concluded in his experimental-therapeutic analysis of "Dreuw's ointment" (salicylic acid, 10 per cent; chrysarobin, 20 per cent; birch tar, 20 per cent; medicinal soft soap, 25 per cent, and wool fat, to make 100 per cent) that chrysarobin is more irritating when incorporated into petrolatum but has a better healing effect on psoriatic lesions than when incorporated in corresponding concentrations into hydrous wool fat. Comparing the healing properties of chrysarobin in petrolatum with corresponding concentration in zinc oxide paste, he observed equally good results but less irritation when zinc oxide paste was used as a base.

In conclusion, it can be said that under the experimental conditions described (1) the reactions of chrysarobin in 1 and in 5 per cent concentration are almost identical; (2) the reactions are more severe if petrolatum is used as a base, and (3) there is no difference in the reaction whether an emulsion base or zinc oxide paste is used as the base. Since the latter is less easily wiped off or smeared by clothes, it seems to be the better choice.

SUMMARY

When chrysarobin comes into contact with oleic acid on the skin it is oxidized to oxychrysarobin, chrysatoxin and chrysophanic acid. Oxychrysarobin is the main therapeutic principle; when chrysophanic acid is formed the therapeutic effect is lost.

Chrysarobin was incorporated in strength of 1, 3, 5 and 10 per cent in the following bases; (1) petrolatum; (2) petrolatum and hydrous wool fat in equal

12. Strakosch, E. A.: Studies on Ointments: III. Ointments Containing Sulfur, Arch. Dermat. & Syph. **47**:216 (Feb.) 1943.

13. Strakosch, E. A.: Studies on Ointments: V. Ointments Containing Resorcinol, Arch. Dermat. & Syph. **48**:393 (Oct.) 1943.

14. Siemens, W.: (*a*) Studien über die Behandlung der Psoriasis, München. med. Wchnschr. **85**:5, 1938; (*b*) Nieuwe Onderzeckingen over de behandeling von psoriasis, Nederl. tijdschr. v. geneesk. **82**:5815, 1938; (*c*) Die experimentell-therapeutische Analyse der Dreuwschen Salbe, Arch. f. Dermat. u. Syph. **179**:580, 1939.

parts; (3) an oxycholesterol-petrolatum ointment base; (4) fatty acid esters of diethanolamine in petrolatum; (5) stearyl alcohol in liquid petrolatum, water and petrolatum, and (6) zinc oxide in talc and petrolatum. Biopsies were performed after one, two, three, seven and ten days, and the action of these ointments on normal human skin was studied histologically.

It was found that (*a*) the reaction of chrysarobin in a 1 and a 5 per cent concentration are almost identical; (*b*) the reactions are more severe if petrolatum is used as a base, and (*c*) there is no difference whether an emulsion base or zinc oxide paste is used as a base.

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STUDIES ON OINTMENTS

VII. ZINC OXIDE PASTES

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The difference between a paste and an ointment is, pharmaceutically speaking, only a gradual one. The former contains more solid substances, which makes it thick. Generally speaking, pastes are mixtures of powders with fats. They are usually credited with some absorptive power, and their usefulness in dermatology is partly attributed to this action. Lassar,[1] who in 1883 introduced pastes into dermatotherapy, praised them for their porosity. While fats are impermeable to serum or water, he argued, the paste, because of the capillary action of its solid constituents, is capable of taking up serum, which will penetrate the applied layer of the paste and, reaching the surface, will be evaporated. This theory, although appealing, can no longer be accepted.

Before this controversial matter is discussed the original formula of zinc paste and later attempted improvements will be given. Lassar's original formula was as follows:

	Gm.
Salicylic acid	2
Petrolatum	50
Zinc oxide	25
Starch	25

Unna,[2] not satisfied with its drying power, recommended the following formula:

	Gm.
Zinc oxide	24
Silica	4
Benzoated oil	12
Benzoinated lard	60

He compared the action of this paste with a blotting paper. He also recommended a soft zinc paste, pasta zinci mollis, consisting of:

	Gm.
Linseed oil	20
Lime water	20
Prepared chalk	30
Zinc oxide	30

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The fourth condensed part of a thesis submitted to the faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirement for the degree of Doctor of Philosophy in Dermatology and Syphilology.

1. Lassar, O.: Ueber Salicyl-Pasten, Monatsh. f. prakt. Dermat. **2**:97, 1883.

2. Unna, P. G., and Trutwin, H.: Handbuch der kosmetischen Chemie, ed. 2, Leipzig, J. A. Barth, 1924, p. 149.

Rapp,[3] fearing that the petrolatum in the paste might lead to irritation, hoped to avoid this by the following prescription:

	Gm. or Cc.
Zinc oxide	54
Talc	4
Wool fat	32
Benzoated cod liver oil	10

Herxheimer [4] used a mixture of 95 per cent petrolatum and 5 per cent cetyl alcohol and octodecyl alcohol instead of pure petrolatum.

Since starch was unobtainable for pharmaceutic use in Austria and Germany during the first world war, talc was substituted for it. It kept its place mostly because of custom, a fact severely criticized by Schmatolla,[5] who attributed many irritations to its use. Lassar after many experiments selected starch because he thought it was least irritating and had the best cooling effect on the skin.

Every constituent of Lassar's paste with the exception of zinc oxide thus has been replaced by various investigators. Zinc oxide has remained because the advantage of its combined physical and bactericidal properties makes it valuable. The bactericidal action of zinc oxide was demonstrated by Haxthausen [6] and Prout and Strickland.[7] Since fats are impermeable to either serum or water, it is difficult to see why the addition of zinc oxide and starch or talc should change that fact. Zinc oxide as well as starch or talc is surrounded by petrolatum and therefore cannot come into direct contact with the serum or sweat. How, then, can they act like filter paper, which is supposed to take up the serum from the skin and give it up by evaporation? Lassar's theory must be wrong, or his paste does not take up serum or water. Veyrières [8] performed some experiments to verify the supposed permeability and porosity of pastes, but from his results he concluded that they possess neither of these properties. His experiments consisted of allowing pastes of varying consistencies to remain in surface contact with aqueous solutions of methylene blue (methylthionine chloride) and eosin for a period of eighteen hours. At the end of this time the interior of the paste was examined for the presence of the dye, but in no case was penetration observed to have taken place. Percival [9] found no ability of Lassar's paste to absorb water or salt solutions. Dietel [10] made similar observations, as did Schmidt-LaBaume and Czetsch von Lindenwald.[11]

Thus it has been shown that zinc oxide paste of the Lassar type is physically unable to absorb water or serum. A possible way to remedy this would be to add emulsifiers or, instead of petrolatum, to use emulsion bases, which are capable of

3. Rapp, R.: Wissenschaftliche Rezeptur und Defektur, Berlin, Julius Springer, 1929.

4. Herxheimer, K.: Ueber Cetosan, München. med. Wchnschr. **78**:195, 1931.

5. Schmatolla, O.: Solidification Points of Fats and Their Importance in Nature, Pharmacol. Ztschr. **79**:1007, 1934.

6. Haxthausen, H.: Some Remarks on the Bactericidal Properties of Zinc Oxide, Brit. J. Dermat. **40**:497, 1928.

7. Prout, W. A., and Strickland, M.: A Comparative Study of the Antiseptic Properties of Certain Ointments Employing Various Bases, J. Am. Pharm. A. **26**:730, 1937.

8. Veyrières: A propos de l'emploi des pastes en dermatologie, Ann. de dermat. et syph. **4**:236, 1923.

9. Percival, G. H.: The Action of Pastes, Brit. J. Dermat. **41**:231, 1929.

10. Dietel, F.: Der feuchte Verband, Deutsche med. Wchnschr. **65**:65, 1939.

11. Schmidt-LaBaume, F., and Czetsch von Lindenwald, H.: Experimentelle und klinische Untersuchungen über Salbengrundlagen, Dermat. Wchnschr. **108**:365, 1939.

taking up serum or water. To demonstrate the validity of this assumption a few simple experiments were performed.

EXPERIMENTAL STUDIES

Desiccated cobalt chloride is blue and turns pink if it comes into contact with water; it was therefore used as an indicator in this study. The following zinc pastes were prepared after each constituent was made water free. Two grams of desiccated cobalt chloride was added to each paste, and the pastes were kept in a desiccator. All pastes were light blue.

	Gm.
1. Zinc oxide	7.5
Starch	7.5
Petrolatum, to make	30.0
2. Zinc oxide	7.5
Talc	7.5
Petrolatum, to make	30.0
3. Zinc oxide	7.5
Starch	7.5
Petrolatum, Hydrous wool fat (equal parts, to make)	30.0
4. Zinc oxide	7.5
Talc	7.5
Petrolatum, Hydrous wool fat (equal parts, to make)	30.0
5. Zinc oxide	7.5
Starch	7.5
Cetyl alcohol	1.5
Petrolatum, to make	30.0
6. Zinc oxide	7.5
Starch	7.5
Fatty acid esters of diethanolamine with petrolatum,[12] to make	30.0
7. Zinc oxide	7.5
Talc	7.5
Fatty acid esters of diethanolamine with petrolatum,[12] to make	30.0
8. Zinc oxide	7.5
Starch	7.5
Oxycholesterol-petrolatum base,[13] to make	30.0

Each paste was applied to an area of about 3 by 3 inches (7.5 by 7.5 cm.) on the forearm of a normal subject for four hours. Pastes with petrolatum as a base were compared with those having an emulsion as a base. Then pastes containing starch were compared with those containing talc. The changes in color are shown in the following tabulation:

Absorption of Water, as Indicated by Change of Color of Cobalt Chloride

Base of Paste	Color After Four Hours
Petrolatum	Blue
Petrolatum–hydrous wool fat	Pink on the edges
Petrolatum plus 5 per cent cetyl alcohol	Pink
Fatty acid esters of diethanolamine in petrolatum [12]	Pink
Oxycholesterol-petrolatum [13]	Pink

COMMENT

It is evident from these experiments that emulsion bases must be used for zinc oxide pastes if the latter are to absorb water or serum. Hydrous wool fat, which usually is a good emulsifier, was inferior for this purpose under the experimental conditions described. The time at which the water-free blue cobalt salt changed to the water-containing pink form was not always the same.

12. The preparation used was hydrosorb, manufactured by the Duke Laboratories, Inc., Stamford, Conn.

13. The preparation used was aquaphor, manufactured by the Abbott Laboratories, North Chicago, Ill.

When pastes with emulsion bases, one containing starch and the other containing talc, were compared it was always found that the starch-containing paste turned pink in a shorter time.

Thus it has been shown that zinc oxide paste of the Lassar type is unable to take up water or serum when a hydrocarbon such as petrolatum is used as a base. If emulsifiers, such as cetyl alcohol, are added or if emulsion bases are used, water-absorbing pastes are obtained. Although the amount of water or serum which will be taken up is certainly small, the process is based not on capillary action, as Lassar believed, but on emulsification.

Starch seems to be better suited than talc, not merely because it is capable of taking up more water but because its surface is more favorable. The small sharply edged talc particles are less favorable for the passage of serum or water than the larger, round starch particles, just as water trickles faster through a layer of gravel consisting of round stones than it does through a layer of fine sand.

Thus it is possible to obtain optimal action of Lassar's zinc oxide paste, which has become indispensable in dermatotherapy. The formula itself is less changed than the explanation of its action.

SUMMARY

Zinc oxide pastes are valuable because of the combined physical and bacteriologic action of the oxide.

Emulsion bases have to be used for zinc oxide pastes if the latter are to absorb water or serum.

Pastes containing starch have a better absorbing power than those containing talc.

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CALCIFICATION AND OSSIFICATION OF STEATOMAS OF THE SCROTUM

REPORT OF A CASE

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Steatoma, or sebaceous cyst, is due to an overproduction of sebum by one or more sebaceous glands while the usual outlet is closed. When this collection remains in situ for years, the peripheral pressure destroys the epithelial lining of the cyst and the sebum may undergo calcareous degeneration.

A few isolated steatomas scattered in various parts of the body are a frequent occurrence. Occasionally one sees large numbers of the pinhead-sized or the pea-sized lesions. The "multiple follicular cutaneous cysts of Bosellini, or steatoma multiplex of Pringle or sebocystomatosis of Günther" were studied extensively by Ormsby and Finnerud,[1] Lisi,[2] Fraccari,[3] Mount [4] and others.

Instances of lesions of large size grouped in large quantities in one region of the body are rare. Similar lesions with extensive calcification seem to be extremely rare.

REPORT OF CASE

A 20 year old man, born in the United States, of Irish ancestry, came to my office on April 22, 1943, complaining of "something very embarrasing" on his scrotum. He had never said a word about it to anybody, but he had to disclose it a week later to his draft board. Besides feeling shame at having contracted some kind of disgraceful disease, he wanted to join the armed forces.

He appeared to be in good general health and had an apparently normal skin except for his scrotum (fig. 1). This was pendulous and studded with hundreds of yellowish red, firm, irregularly round, smooth nodules ranging in size from that of the head of a pin to that of a pea or a bean. Only the anterior aspect of the scrotum was involved. The posterior aspect of it, as well as the rest of the body, was completely free of lesions.

The lesions had been gradually appearing for about ten years.

A roentgenogram (fig. 2) showed that most of the nodules were filled with calcareous material.

One large-sized lesion was excised, and sent to Dr. B. E. Clarke, pathologist of the Rhode Island Hospital, for study.

Pathologic Examination.—Gross Description: The specimen consisted of a rounded portion of tissue 1.3 cm. in diameter. A part of the surface was covered with epidermis. In the underlying fibrous tissue were small pockets containing a white grumous material. This material was gritty and apparently contained calcium.

Microscopic Description: The surface epidermis was intact but thin and its lower border rather straight. The underlying corium was dense and hyaline. Scattered through this hyaline tissue were masses of acellular material that frequently stained blue with hematoxylin, which indicated the presence of calcium. This material was in direct contact with the surrounding hyaline connective tissue. Nowhere was there any evidence of epithelium.

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1. Ormsby, O. S., and Finnerud, C. W.: Steatocystoma Multiplex, Arch. Dermat. & Syph. **22**:882 (Nov.) 1930.

2. Lisi, F.: Nevo cistico tricosebaceo diffuso del tronco; steatocisti multiple dei follicoli pilo-sebacei (Bosellini); steatocistoma multiplex (Pringle); sebocistomatosi (Günther), Gior. ital. di dermat. e sif. **73**:1325, 1932.

3. Fraccari, B.: Un caso di steatocisti multiple dei follicoli pilo-sebacei (Bosellini); sebocistomatosi (Günther), Gior. ital. di dermat. e sif. **77**:977, 1936.

4. Mount, L. B.: Steatocystoma Multiplex, Arch. Dermat. & Syph. **36**:31 (July) 1937.

Strangely, there was no foreign body reaction to this calcified material. In one of the larger masses there was ossification. Except for the osteoblasts and bone cells here, the material was distinctly acellular.

Particularly interesting were spots in which numerous small calcified areas appeared within the hyalinized connective tissue. These varied in diameter from about 20 microns upward. They appeared to be the result of a change in glands that later lost their epithelial lining.

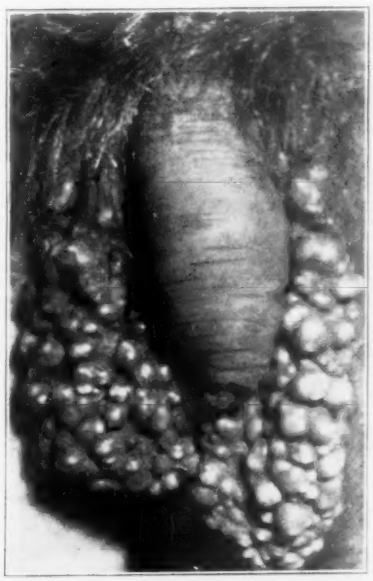

Fig. 1.—Anterior aspect of the scrotum studded with cysts.

Fig. 2.—Roentgenogram showing extensive calcification.

Dr. Clarke was of the opinion that the larger masses were formed by coalescence of these smaller ones. It seems probable that the primary lesion was the hyaline change in the corium, which later underwent degeneration and became calcified. At any rate, there was no evidence in these sections in favor of the idea that these were originally epithelium-lined spaces.

Diagnosis.—A diagnosis of hyalinization, calcification and ossification of the skin of the scrotum was made.

The patient was accepted by the Army without reservations or suggestions about therapy.

COMMENT

From a survey of the literature made by the previously mentioned authors, the only instance of steatomas of considerable size grouped in large numbers in one area (scalp) is the case of Fraccari.[3]

A case apparently identical with the one herein reported was published by Dracoulidès,[5] of Athens, Greece. At the meeting of April 7, 1938 of the Lyon section of the Société française de dermatologie et de syphiligraphie he presented two photographs, presumably of an Athenian man, aged 53, showing one hundred and thirty two sebaceous-epidermic cysts scattered on the anterior and posterior aspects of the scrotum. The disease began twenty years previously, and the last

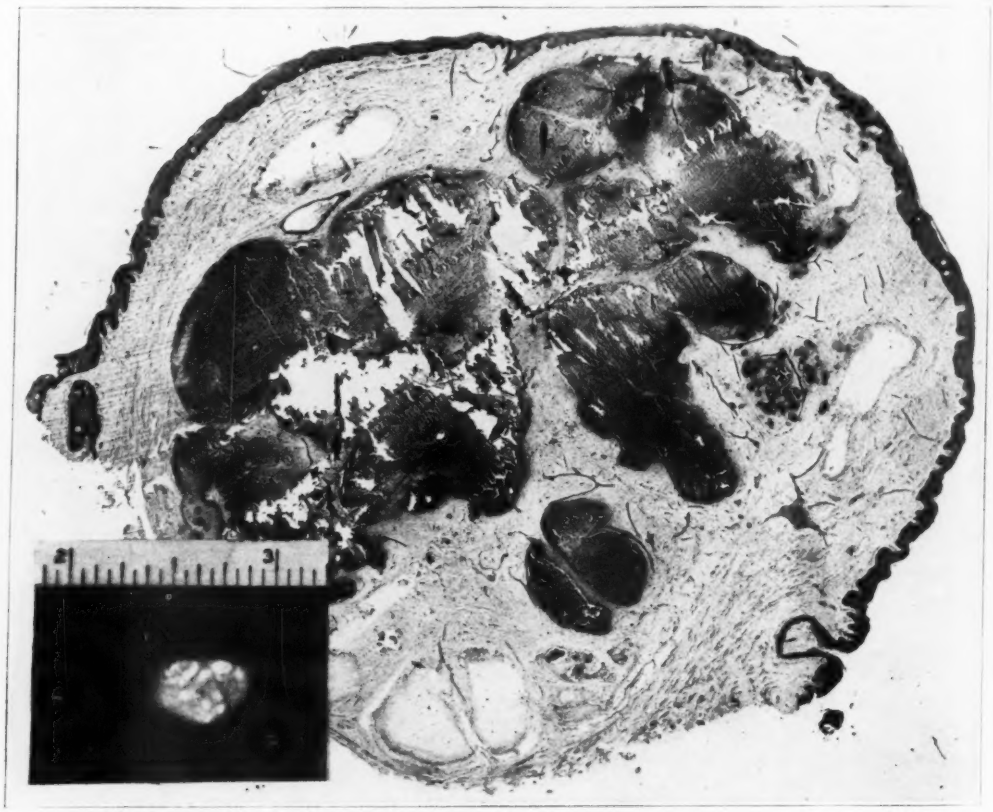

Fig. 3.—Gross appearance of a cut nodule and a low power photomicrograph showing an old cyst in which the epithelium had disappeared and the spaces are filled with partly calcified and some ossified amorphous material.

lesion had been present for six months. The lesions were described as round, with a doughy, sebaceous content, gradually becoming irregular and lobulated because of massing of calcerous concretions. The size varied from that of a small pea to that of a walnut.

Dracoulidès said that all the cysts were calcified and that he intended to remove them surgically. No investigation, however, was made to determine their histologic structure.

5. Dracoulidès, N. W.: 132 loupes sébacéo-épidermiques calcifiées évoluées sur un scrotum pendant 20 années, Bull. Soc. franç. de dermat. et syph. **45**:648, 1938.

Fraccari [2] discussed the cause of sebocystomatosis and suggested its relation to acne and particularly to endocrinopathologic acne. It may be a valuable suggestion, especially for the type known as cystic acne. However, my apparently healthy adolescent patient did not show any trace of acne of any type.

Lisi [2] discussed milium, atheroma, naevus syringoadenomatosus papilliferus and trichoepithelioma and concluded that this disease is of nevic origin.

Because of the extensive calcification and the ossification in my case, the observation of Dracoulidès and mine seem to concern a separate variety of sebocystomatosis. The possibility of a nevic origin is suggestive.

SUMMARY

A case is reported of calcification and ossification of steatomas of the scrotum. Lesions so numerous and large, grouped in one area of the body, so extensively calcified and with ossified areas are rarely encountered. Because of the extensive calcification and points of ossification it seems to be a distinct variety of what is known as steatoma multiplex or sebocystomatosis.

Most likely this is an ectodermal disease of nevic origin.

Surgical excision is the treatment of choice.

122 Waterman Street.

RATIONAL PHARMACEUTIC TREATMENT OF DISEASES OF THE SKIN

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NEW YORK

I. SUGGESTED SUBSTITUTE FORMULAS FOR WHITE OINTMENT AND YELLOW OINTMENT U. S. P. XII.

The two official ointment bases, white ointment U. S. P. and yellow ointment U. S. P., are not worthy of places in the therapy of the prescribing dermatologist. Their only virtue lies in their freedom from rancidity. Their formulas disregard the niceties of prescription writing. They take no account of the level of assumed activity of the prescribed ointment, whether epidermic, endodermic or diadermic. It is difficult to incorporate powders into these bases. No provision is made for adding liquid petrolatum. The predominance of mineral grease reduces the value of these ointment bases for eruptions of the skin or scalp accompanied by oozing or moisture. The emulsifying characteristics of animal fats, such as lard, are lacking.

The suggested substitutes for the official bases consider the intended level of action. Is the ointment intended solely for the outermost layers of the epidermis? If so, mineral oils and hydrogenated fats and fatlike products are excellent vehicles.

Suggested Formula for Ointment Base Intended for Penetration (?) into the Layers of the Outer Skin (Epidermic)

	Gm. or Cc.
Light liquid petrolatum	5
Wool fat	5
White petrolatum, to make	100

Is the ointment intended for penetration (?) into the skin? Increased proportions of animal fats are provided, with reduction of the mineral grease and fatlike products.

Suggested Formula for Ointment Base Intended for Penetration (?) into the Layers of the Skin (Endodermic)

	Gm. or Cc.
Light liquid petrolatum	5
Wool fat	30
White petrolatum, to make	100

Note: The light liquid petrolatum is prescribed because it permits the pharmacist to moisten the powdered ingredients of the prescription. Water may be ordered to dissolve water-soluble ingredients.

Suggested Formula for Endodermic Ointment of Boric Acid

	Gm. or Cc.
Boric acid, in fine powder	10
Water, to dissolve	10
Wool fat	30
White petrolatum, to make	100

II. SUGGESTED SUBSTITUTE FORMULAS FOR OINTMENT OF BENZOIC AND SALICYLIC ACID N. F. VII

The rationale of the application of ointment of benzoic and salicylic acid N. F. (Whitfield's ointment) for the treatment of all types of ringworm of the toes and toe interspaces is open to criticism. There is no pharmaceutic reason to include benzoic acid. A concentration of salicylic acid of 6 per cent is on the borderline for

keratolytic action; less than 6 per cent acts as a keratoplastic. One who prescribes the ointment desires either keratoplastic action or keratolytic action. A made to measure prescription designed for the individual patient can be written. The patient is assured of the needed action by selection of the proper concentration of the chemical reducing agent, salicylic acid.

This comment is aside from the fact that Whitfield did not intend the ointment bearing his name to be the sole medicament in the treatment of the tinea of the toes and toe interspaces. In the treatment of old infections Whitfield used this method: After being trimmed, the skin is painted with a solution consisting of chrysarobin, 20 per cent, and sulfuric ether and acetone, equal parts of each to make 100. This is allowed to dry, after which the feet are covered with a pair of cotton socks. In the evening the solution is washed off and the feet dressed with benzoic acid, 5 per cent, salicylic acid, 3 per cent; petrolatum, 8 per cent, and coconut oil, to make 100 per cent.

Rational pharmaceutics of ringworm of the toes and toe spaces requires keratolytic agency of salicylic acid for the hyperkeratotic lesions in cases of long duration. The action is sought for the depth of the skin-endodermic ointment base or vehicle.

Suggested Formula for Hyperkeratotic Lesions of Ringworm of the Toes and Toe Interspaces (1)

	Gm. or Cc.
Salicylic acid	6
Light liquid petrolatum	5
Wool fat	12
White petrolatum, to make	100

Suggested Formula for Hyperkeratotic Lesions of Ringworm of the Toes and Toe Interspaces (2)

	Gm. or Cc.
Chrysarobin	5
Chloroform, to make	100

Experiments in the laboratory and the clinic indicate the efficacy of certain volatile drugs in inhibiting the growth of tinea organisms. Phenyl salicylate, thymol, chloral hydrate, menthol and camphor to no more than a total of 2 per cent may be incorporated in the salicylic acid ointment formula.

Ringworm of the toes and toe spaces with denudation of the skin does not require the keratolytic action of salicylic acid. Antiseptic drugs are needed. A liquid is better than an ointment.

Suggested Formula for Denuded Lesions of Ringworm of the Toes and Toe Interspaces

	Cc.
Tincture of aconite N. F.	20
Tincture of iodine U. S. P.	30
Alcohol, to make	100

Prevention of reinfection of ringworm of the toes and toe interspaces is part of the therapeutic regimen.

Suggested Formula for Preventive Powder for Ringworm of the Toes and Toe Interspaces

	Gm.
Phenyl salicylate	1
Chloral hydrate	1
Sterilized purified siliceous earth, to make	100

III. SUGGESTED SUBSTITUTE FORMULA FOR PASTE OF ZINC OXIDE N. F. 1942

The official paste of zinc oxide has a number of failings in the light of rational pharmaceutic therapeutics for diseases of the skin. It should be modified by the prescribing physician. Two suggestions are made. The present official formula

results in a paste that is hard, difficult to apply, more difficult to remove from the skin and still more difficult to remove from hairy parts. The starch incorporated has no action on the skin or the products of cutaneous irritation, such as fluids. The first suggestion for change for the prescription writer is to include boiled starch instead of starch. The formula will be for immediate use and will not have staying qualities in the jar, but it will have the desired action on the skin and will be easy to apply and easier to remove. The second suggested change is the inclusion of an animal fat, such as lard or benzoinated lard. The advantages of the animal fat include the natural emulsifying fraction permitting the absorption of products of cutaneous irritation, such as fluids.

Suggested Formula for Zinc Oxide and Starch Paste

	Gm. or Cc.
Starch	25
Water	50
(Rub starch in cold water until smooth; heat and stir until it becomes translucent)	
Zinc oxide	25
Lard, or benzoinated lard	50

It is not practical to protect the starch paste from mold formation.

BOILED STARCH FOR STARCH BATHS

This may be the proper place to mention the inclusion of starch in the bath water. Many physicians order starch baths. The patient usually asks how much starch to how much water. He is directed to place a pound of starch in the conventional tubful of warm water. The results are rarely as anticipated. The reason for failure is the incomplete direction. The patient should be instructed to boil the starch. The starch granules must be burst to release the colloidal acting materials. Either corn starch or laundry starch is taken. Half a pound to 1 pound (0.25 to 0.5 Kg.) is placed in 1 or 2 quarts (1 or 2 liters) of cold water. The starch is rubbed in the palms until smooth. The vessel is then placed over an open flame and heated, with constant stirring. Soon the color changes, and the white liquid becomes a translucent paste. It is removed from the flame and allowed to cool before it is added to the tub of warm water.

Boiled starch may be applied as a dressing to the skin or scalp prior to immersion into the tub of water. The almost cooled starch paste is packed on the part and allowed to harden as it continues to cool. When pressure is felt, the tub bath is taken. The starch is removed from the skin by contact with water. No soap is required when boiled starch is used in bathing, and the body need not be rinsed with clear water. A film of starch may adhere after the skin is patted dry.

VEHICLE FOR EXTERNAL APPLICATION OF SULFONAMIDE COMPOUNDS

The application of sulfonamide compounds locally in dermatology is fast fading from popularity. Through loopholes in sanitary codes, the sulfonamide compounds forbidden to be sold for internal use may be offered for sale for external application. Prescribing physicians may require a suitable vehicle for external application of the compounds. Boiled starch offers an excellent base.

	Gm.
Starch	10
Water, to make	100
Rub the starch in cold water until smooth; heat with constant stirring until translucent; cool; add the sulfonamide compound, and mix.	

18 East Eighty-Ninth Street.

DERMATOLOGIC SIGNIFICANCE OF TISSUE EOSINOPHILIA

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Eosinophilic leukocytes are present in the tissue infiltrate of various dermatologic disturbances. This study was undertaken in an attempt to determine whether there is any relationship between eosinophilia in the tissues and eosinophilia in the blood in some of the dermatologic diseases which cause tissue eosinophilia. In the microscopic study of routine dermatologic sections, at times numerous eosinophils with monolobed [1] nuclei are found, while in other sections the eosinophils have nuclei which are bilobed or trilobed. In looking over the literature we found no mention of the relative importance of these two types of eosinophils. Little work apparently has been done to correlate the type of eosinophils with the disease entity.

The earliest reference to the eosinophilic leukocyte is attributed to T. W. Jones,[2] who described coarsely granular cells in the blood as early as 1846. In 1861, Förster [3] mentioned similar cells in the blood; however, the existence of the eosinophil as a definite morphologic entity was established by Schultze [4] in 1865. Ehrlich [5] did considerable work on the eosinophilic leukocyte, and in 1878 and 1879 he first demonstrated that the eosinophils constituted a distinct variety of leukocyte. Ehrlich's theory of the origin of the eosinophilic leukocyte is still the most generally accepted one.

ORIGIN OF EOSINOPHILS

The origin of the eosinophils circulating in the blood has been in dispute ever since these cells were first identified. There can be no doubt that at least a portion of them originate in the bone marrow, and Ehrlich's original theory was that all eosinophilic leukocytes originate from the bone marrow and enter the circulation as mature cells. Ehrlich's theory has been disputed by many investigators. Van der Stricht [6] (1892) emphasized regeneration by mitosis of preexisting elements of eosinophils (homoplastic theory), and it was his belief that this was the only

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1. By a monolobed nucleus is meant one which is oval, kidney shaped or band shaped.

2. Jones, T. W.: The Blood-Corpuscle Considered in Its Different Phases of Development in the Animal Series, Phil. Tr. Roy. Soc., London **136**:63-106, 1846.

3. Förster: Fall von vorwiegend lymphatischer Leukämie, Virchows Arch. f. path. Anat. **20**:399-402, 1861.

4. Schultze, M.: Ein heizbarer Objecttisch und seine Verwendung bei Untersuchungen des Blutes, Arch. f. mikr. Anat. **1**:1-43, 1865.

5. Ehrlich, P. C.: Ueber die specifischen Granulationen des Blutes, Arch. f. Physiol., 1879, pp. 571-579.

6. Van der Stricht, O.: Nouvelles recherches sur la génèse des glogules rouges et des globules blancs du sang, Arch. de biol., Paris **12**:199, 1892.

method of eosinophilic regeneration. Brown [7] (1898) stated the belief that eosinophils arise, in some instances at least, by direct transformation from neutrophils (heteroplastic theory). He based his conclusion on the fact that in a patient with trichinosis a biopsy of muscle showed many neutrophils with many typical eosinophils and cells which he regarded as transitional between the two. Two weeks later, another biopsy showed a greatly increased number of eosinophils. He interpreted this as evidence that eosinophils arose from polymorphonuclear leukocytes. Pappenheim [8] (1899 and 1905) supported the contention that eosinophils arose from mitosis of preexisting eosinophils, although he admitted formation of eosinophils from nongranular elements (rabbit embryo). Pröscher [9] (1905) demonstrated that eosinophils were produced *in loco* from the peritoneal endothelial cells and showed a progressive change from eosinophilic granulated endothelial cells to mononuclear and lobulated eosinophils. In his experiments he used guinea pigs and injected intraperitoneally an aqueous extract made from Taenia saginata.

Maximow [10] (1907) and Grawitz [11] (1911) emphasized the homoplastic method of differentiation. A little later heteroplastic differentiation was mentioned more frequently. Howard and Perkins [12] (1902) reported local development from large mononuclear cells, plasma cells and even smooth muscle fibers. Pappenheim [13] (1905) and Dominici [14] (1909) admitted heteroplastic regeneration of eosinophils in tissues. Browning [15] (1905) found eosinophils in the connective tissue, liver and thymus of 10 week old human fetuses, and he expressed the opinion that these occurred before the formation of bone marrow. Gütig [16] (1907) postulated two types of eosinophils, tissue eosinophils and blood eosinophils. He regarded the granules of the former as fragments of phagocytosed erythrocytes and the latter as true protoplasmic differentiations (endogenous formations). Weill [17] (1913 and 1919) observed both homoplastic and heteroplastic development of eosinophils. Barbano [18] (1914) reported heteroplastic regeneration from small and large lymphocytes. He also observed differences in the staining reactions of eosinophilic granules in the case of tissue (local) eosinophilia, but this was thought to indicate

7. Brown, T. R.: Studies on Trichinosis, with Especial Reference to the Increase of the Eosinophilic Cells in the Blood and Muscle, the Origin of These Cells and Their Diagnostic Importance, J. Exper. Med. **3**:315-348, 1898.

8. Pappenheim, A.: Vergleichende Untersuchungen über die elementare Zusammensetzung des rothen Knochenmarke einiger Säugethiere, Virchows Arch. f. path. Anat. **157**:19-76, 1899.

9. Pröscher, F.: Ueber experimentelle Erzeugung von eosinophilen Exsudaten, Folia haemat. **2**:543-549, 1905.

10. Maximow, A.: Experimentelle Untersuchungen zur postfötalen Histogenese des myeloiden Gewebes, Beitr. z. path. Anat. u. z. allg. Path. **41**:122-166, 1907.

11. Grawitz, E.: Klinische Pathologie des Blutes, ed. 4, Leipzig, Georg Thieme, 1911.

12. Howard, W. T., Jr., and Perkins, R. G.: Observations on the Origin and Occurrence of Cells with Eosinophile Granulations in Normal and Pathological Tissues, Johns Hopkins Hosp. Rep. **10**:249-281, 1902.

13. Pappenheim, A.: Zur Frage der Entstehung eosinophiler Leukozyten, Folia haemat. **2**:166-168, 1905.

14. Dominici, H., cited by Downey, H.: Handbook of Hematology, New York, Paul B. Hoeber, Inc., 1938, pp. 1-184.

15. Browning, C. H.: Observations on the Development of the Granular Leucocytes in the Human Foetus, J. Path. & Bact. **10**:145-158, 1905.

16. Gütig, K.: Ein Beitrag zur Morphologie des Schweineblutes, Arch. f. mikr. Anat. **70**:629-694, 1907.

17. Weill, P.: Ueber die Bildung von Leukozyten in der menschlichen und tierischen Thymus des erwachsenen Organismus, Arch. f. mikr. Anat. **83**:305-360, 1913; Ueber die Bildung von granulierten Leukozyten in Karzinomgewebe, Virchows Arch. f. path. Anat. **226**:212-228, 1919.

18. Barbano, C.: Die lokale Eosinophilie, Virchows Arch. f. path. Anat. **217**:402-452, 1914.

merely that the granules of tissue eosinophils were variable in their staining capacity with eosin. He did not draw any conclusion as to the origin of the eosinophilic granules. Herzog [19] (1914 and 1915) described development from lymphocytes, adventitial cells and large wandering cells. Downey [20] (1915) described heteroplastic development of all three types of granular leukocytes (eosinophils, basophils and neutrophils) from nongranular cells in an active process in the bone marrow of adult guinea pigs. He concluded that the granules of the eosinophilic leukocyte of the bone marrow were endogenous formations. He observed the gradual differentiation of these granules from a basophilic cytoplasm. Ringoen [21] (1915) showed that in the bone marrow of mammals the eosinophilic granules were real endogenous formations. He found no evidence which would even suggest that the eosinophilic granules originated from hemoglobin. Bayne-Jones [22] (1916) studied a case of postpneumonic pleural effusion in which 45 per cent of the cells in the exudate were eosinophils. Many of the eosinophils in the exudate were of the mononuclear type. The patient's blood exhibited a slight eosinophilia but did not contain any mononuclear eosinophils. The shape of the eosinophils in the pleural exudate strongly suggested a local origin outside the bone marrow. Biggart [23] (1932) injected foreign proteins subcutaneously and intramuscularly into animals and studied the resulting infiltrate. He concluded that the tissue eosinophils were not formed *in loco* but migrated from the blood stream.

FUNCTION OF EOSINOPHILS

The fact that eosinophils are present to a greater or less extent in the tissue infiltrate of certain dermatoses and entirely absent in the tissue infiltrate of other dermatoses has never been satisfactorily explained. Eosinophils are normally found throughout the gastrointestinal tract, especially in the mucosa, and they are abundant in the lactating breast.

Schwarz [24] (1914) stated the belief that the products of protein destruction in an exudate undergoing absorption may constitute the eosinotactic substance that produces both the general and the local eosinophilia. According to Baar [25] (1927), eosinophilia of the blood indicates nonspecific sensitization to autogenous or foreign proteins. Coates and Ersner [26] (1929) considered the eosinophil a factor in inflammations that are irritative rather than infective. In 1930, Bezançon and Bernard [27] stated that the eosinophil is a connective tissue cell which is associated with the

19. Herzog, G.: Ueber adventitielle Zellen und über die Entstehung von granulierten Elementen, Verhandl. d. deutsch. path. Gesellsch. **17**:562-565, 1914; Experimentelle Untersuchungen über die Einheilung von Fremdkörpern, Beitr. z. path. Anat. u. z. allg. Path. **61**:325-449, 1915.

20. Downey, H.: The Origin and Development of Eosinophil Leucocytes and of Haematogenous Mast Cells in the Bone Marrow of Adult Guinea Pigs, Folia haemat. **19**:148-206, 1915.

21. Ringoen, A. R.: The Origin of the Eosinophil Leucocytes of Mammals, Folia haemat. **27**:10-68, 1915.

22. Bayne-Jones, S.: Pleural Eosinophilia with Report of a Case, Bull. Johns Hopkins Hosp. **27**:12-16, 1916.

23. Biggart, J. H.: Some Observations on the Eosinophile Cell, J. Path. & Bact. **35**: 799-816, 1932.

24. Schwarz, E.: Die Lehre von der allgemeinen und örtlichen Eosinophilie, Ergebn. d. allg. Path. u. path. Anat. **17**:138-790, 1914.

25. Baar, H.: Allergische Eosinophilie, Monatschr. f. Kinderh. **37**:444-448, 1927; reviewed, Folia haemat. **40**:485, 1930.

26. Coates, G. M., and Ersner, M. S.: Occurrence of Eosinophils in the Mucous Membrane of the Maxillary Sinus in Asthmatic Patients, Tr. Sect. Laryng., Otol. & Rhin., A. M. A., 1929, pp. 97-107.

27. Bezançon, F., and Bernard, E.: L'eosinophilie dans l'asthme, ses équivalents et ses parentés morbides, Ann. de méd. **27**:204-233, 1930.

repair that takes place at the site of injury. They thought that local eosinophilia occurs first at the site of reaction and that eosinophilia in the blood occurs secondarily. Campbell, Drennan and Rettie [28] (1935) attempted to correlate local eosinophilia and blood eosinophilia in the guinea pig. They found that local eosinophilia and blood eosinophilia are frequent but not constant accompaniments of allergic inflammation in guinea pigs and also that local eosinophilia cannot be produced by the injection of foreign proteins unless allergic reactions occur. Similarly, blood eosinophilia is produced only on reinjection of the foreign protein under conditions compatible with the occurrence of an allergic reaction. Hall [29] (1935) found that in aneosinophilic guinea pigs there is a comparative absence of an eosinophilic response to homologous protein substances and bacterial products. Kirk [30] (1938) reviewed several different dermatologic entities associated with a blood eosinophilia and found that in his series there were 24 cases of dermatitis herpetiformis with an average eosinophil count of 16 per cent of the total number of leukocytes, 40 cases of mycosis fungoides with counts ranging as high as 25 per cent, 60 cases of pemphigus (type not classified) with counts as high as 22 per cent, 100 cases of scarlet fever with eosinophil counts as high as 17 per cent and 15 cases of secondary syphilis in which the percentage of eosinophils varied from 0 to 12. He concluded that a blood eosinophilia of 10 per cent or less is not diagnostic of any disease. Kraft [31] (1941) studied 200 clinic patients showing an eosinophil count of the blood of more than 9 per cent. Five, or 2.5 per cent, of these patients had dermatosis. He did not classify the type of dermatosis present.

Local eosinophilia has been studied after the injection of foreign proteins by Schlecht and Schwenker [32] (1912), who emphasized that the local eosinophils came from the blood stream and that they were not of local origin. Several other investigators have studied this same problem and found that local eosinophilia could be produced by the injection of a foreign protein but that this local eosinophilia had a direct relationship to the degree of blood eosinophilia. Goodman [33] (1941) produced blisters artificially by the local application of cantharides and solid carbon dioxide to patients with dermatitis herpetiformis and pemphigus. These blisters were then excised and studied histologically. He found that in patients with dermatitis herpetiformis without eosinophils in the blood as well as in normal patients with a normal number of eosinophils in the blood there was no eosinophilia in the artificially produced blisters but that in patients with dermatitis herpetiformis with eosinophilia in the blood there was an eosinophilia in the artificially produced blisters also.

Eosinophils do show chemotropism. Ingraham and Wartman [34] (1939) obtained eosinophils from a patient with eosinophilic leukemia and from a patient with dermatitis herpetiformis. They studied the chemotaxis in vitro with bacteria, Trichinella spiralis and Witte's peptone as sources of attraction. They demonstrated that in vitro eosinophils show the same degree of positive chemotropism as do neutrophils.

28. Campbell, A. C. P.; Drennan, A. M., and Rettie, T.: The Relationship of the Eosinophile Leucocyte to Allergy and Anaphylaxis, J. Path. & Bact. **40**:537-548, 1935.

29. Hall, I. W.: Eosinophiles and Homologous Proteins, J. Path. & Bact. **40**:319-322, 1935.

30. Kirk, R. C.: The Causes of Eosinophilia, Internat. Clin. **5**:219-233, 1942.

31. Kraft, B.: Significance of Blood Eosinophilia in Group of Ambulatory Patients, J. Indiana M. A. **34**:249-250, 1941.

32. Schlecht, H., and Schwenker, G.: Ueber die Beziehungen der Eosinophilie zur Anaphylaxie, Deutsches Arch. f. klin. Med. **108**:405-428, 1912.

33. Goodman, M. H.: The Artificial Blister in the Study of Eosinophiles with Particular Reference to Dermatitis Herpetiformis, J. Invest. Dermat. **4**:349-364, 1941.

34. Ingraham, E. S., and Wartman, W. B.: Chemotropism of Human Eosinophilic Polymorphonuclear Leukocytes, Arch. Path. **28**:318-322 (Sept.) 1939.

In 1922, McDonald and Shaw [35] demonstrated that the eosinophilic myelocytes showed phagocytic power and that eosinophils with simple indented nuclei were twice as active, while eosinophils with two, three and four lobulations of the nuclei were even more phagocytic. Strumia and Boerner [36] (1937) showed that eosinophils were phagocytic but that they were less actively phagocytic than neutrophils or monocytes.

The individual eosinophilic granules probably have a definite function. Olson [37] (1931) prepared a solution of pure eosinophilic granules and showed that these granules when added to a specific protein and then passed through a Berkefeld filter yielded a filtrate which contained a specific sensitizing substance.

METHOD OF STUDY

All the cases of dermatitis herpetiformis and pemphigus vegetans in which we had obtained histologic sections were studied, together with a large series of cases in which a clinical diagnosis of atopic dermatitis or neurodermatitis had been made. The histories were reviewed in each of these cases especially for data on blood counts and for a personal or family history of allergy. In many cases no differential blood counts had been made, and in others blood counts had not been made recently. In most cases there was a definite statement indicating whether the patient had been questioned as to allergy or not; however, in some cases this was not true, and in other cases the patient could not make a definite statement.

In each case a differential count of the cells in the infiltrate was made with the oil immersion objective. A ruled piece of cellophane was placed in the ocular of the microscope so that the ruled lines were projected on the microscopic field to make the count more accurate. A total of 200 cells was counted in each case, and the per cent of monolobar or bilobar eosinophils was recorded. In a few cases more then one biopsy was performed within a week or so. The differential cell counts in these cases corresponded closely.

One hundred and fifty-eight cases were studied. These included 76 cases of localized neurodermatitis, 9 cases of exudative neurodermatitis, 61 cases of atopic dermatitis, 9 cases of dermatitis herpetiformis and 3 cases of pemphigus vegetans. These entities were chosen because it was felt that the incidence of tissue eosinophilia was rather high in these diseases and that they afforded a good opportunity for the special study of tissue eosinophils.

LOCALIZED NEURODERMATITIS (LICHEN VIDAL)

Seventy-six cases of localized neurodermatitis were studied. In each of these cases the dermatitis was limited to one or two small areas. The most common sites of involvement were the neck and extremities. In the 22 cases in which a differential blood count was made the percentage of eosinophils was as follows: 0 to 1.9 in 6 cases, 2 to 4.9 in 9 cases, 5 to 9.9 in 4 cases, 10 to 19.9 in 2 cases and 35 in 1 case. In 9 of the 22 cases the percentage of eosinophils was 3 or more. In 5 of the 9 cases the patients had superimposed contact dermatitis which was due to strong lotions or ointments. In 1 of the remaining 4 cases there was a family history of allergy. In the remaining 3 cases there was no history of allergy. The results of this study indicate that the percentage of eosinophils in the blood is not increased in cases of uncomplicated lichen simplex chronicus.

As the tissue infiltrate was scanty, it often was necessary to examine two or more sections in order to count a total of 200 cells. In 62, or 81.6 per cent, of the 76 cases no eosinophils were found in the tissue. Undoubtedly, at least 1 eosinophil could have been found in most of the cases if several hundred cells had been counted. In the 14 cases in which eosinophils were found in the infiltrate, the

35. McDonald, S., and Shaw, A. F. B.: Persistent Eosinophilia with Splenomegaly, Brit. M. J. **2**:966-971, 1922.

36. Strumia, M. M., and Boerner, F.: Phagocytic Activity of Circulating Cells in the Various Types of Leukemia, Am. J. Path. **13**:335-349, 1937.

37. Olson, B.: Unpublished thesis, Mayo Foundation, 1931.

percentage of these cells was as follows: 0.1 to 0.9 in 4 cases, 1 to 2.9 in 7 cases, 5 to 6.9 in 2 cases and 9 to 15 in 1 case. More than 2 per cent of eosinophils were present in 5 of the 14 cases. In 8 of the 14 cases there was a predominance of binuclear eosinophils, and in 3 cases there was an equal number of mononuclear eosinophils. In 3 of the cases there was an equal number of mononuclear and binuclear eosinophils. Eosinophils with more than two nuclei were not found in any of the cases.

In 5 cases there was an element of contact dermatitis when the biopsy was performed. In each of these cases the blood eosinophilia was considerably higher than the tissue eosinophilia. In 1 case the percentage of eosinophils in the blood was as high as 35, and in this particular case there were no eosinophils in the tissue. In cases of contact dermatitis the blood eosinophils apparently show more of a response than do the tissue eosinophils.

In 15, or 19.7 per cent, of the 76 cases there was a definite personal or familial history of allergy.

EXUDATIVE NEURODERMATITIS [38]

In the cases of exudative neurodermatitis the lesions were multiple and disseminate but not perfectly symmetric. They consisted of grouped papulovesicles, vesicles and crusted lesions.

Nine cases of exudative neurodermatitis were studied. In 1 case a differential blood count was not made; in the remaining cases the percentage of eosinophils in the blood was as follows: 0 to 1.9 in 1 case, 2 to 4.9 in 2 cases, 5 to 9.9 in 3 cases and 10 to 19.9 in 2 cases. In all but 1 case a differential blood count revealed more than 3 per cent of eosinophils. Tissue eosinophilia was present in 8 of the 9 cases. The percentage of eosinophils in the tissue in these 8 cases was as follows: 1.0 to 2.9 in 5 cases, 3 to 4.9 in 1 case, 5 to 6.9 in 1 case and over 9 in 1 case. Binuclear eosinophils predominated over mononuclear eosinophils in 6 cases, and in 2 cases there were equal numbers of monolobed and bilobed eosinophils. In no case was there an excess of monolobed eosinophils.

In 3 cases there was a personal or family history of allergy.

ATOPIC DERMATITIS (DISSEMINATE NEURODERMATITIS)

Sixty-one cases of atopic dermatitis were studied. A differential blood count was not made in 6 of these cases. One differential blood count was made in each of 53 cases; in each of the remaining 2 cases a differential blood count was made on two occasions. In the 53 cases in which only one differential blood count was made, the percentage of eosinophils was as follows: 0 to 1.9 in 4 cases, 2 to 4.9 in 14 cases, 5 to 9.9 in 12 cases, 10 to 19.9 in 18 cases, 20 to 29.9 in 4 cases and 30 to 40 in 1 case. In the 2 cases in which a differential blood count was made on two occasions, the percentage of eosinophils was as follows: 5 and 9 in 1 case and 15 and 1 in the other.

Biopsy was performed on one occasion in each of 59 cases. In each of the 2 remaining cases, biopsy as well as a differential blood count was performed on two occasions. In all but 12 cases eosinophils were present in the tissue infiltrate. Undoubtedly in these 12 cases some eosinophils could have been found if enough cells had been counted. In the cases in which only one biopsy was performed the percentage of tissue eosinophils was as follows: 0.1 to 0.9 in 9 cases, 1 to 2.9 in 21

38. In cases in which the lesions were classified as exudative neurodermatitis multiple lesions were distributed on the trunk and extremities. These lesions were not situated at the sites of predilection for atopic dermatitis.

cases, 3 to 4.9 in 7 cases, 5 to 6.9 in 7 cases, 7 to 8.9 in 1 case and 9 to 12 in 2 cases. In the 2 cases in which a biopsy was performed on two occasions, the percentage of tissue eosinophils was 9 and 7.5 in 1 case and 3.5 and 0 in the other case.

As previously stated, biopsy disclosed tissue eosinophilia in 49 of the 61 cases of atopic dermatitis. Monolobar eosinophils predominated in 12 cases, and bilobar eosinophils predominated in 32 cases. In 5 cases there was an equal number of bilobar and monolobar eosinophils.

In 5 cases, eosinophils with three and more lobes to their nuclei were present. In these cases there was no relationship between the degree of eosinophilia in the blood and that in the tissue except that in no case were eosinophils with trilobed nuclei present unless eosinophils with monolobed or bilobed nuclei were also present.

In 31, or 50.8 per cent, of the 61 cases there was a family or personal history of allergy. In 11 cases the history was inadequate regarding allergic manifestations. In the remaining 19 cases it was stated definitely that there was no knowledge of any allergic manifestations among the patients or members of their families.

DERMATITIS HERPETIFORMIS

We experienced considerable difficulty in making a differential count of the cells in the tissue infiltrate in many cases of dermatitis herpetiformis because the cells, especially the neutrophils, were so decidedly acidophilic that we found it impossible to make an accurate differential count. This was true especially when the cells were closely packed together. We started out with 15 cases but had to discard 6 when we found it impossible to make an accurate count after studying several sections in each case.

No differential leukocyte count was made in 4 of the 9 cases. In the remaining 5 cases the percentage of eosinophils in the blood was as follows: 0 to 1.9 in 1 case, 2 to 4.9 in 2 cases, 5 to 9.9 in 1 case and 30 to 40 in 1 case.

Eosinophils were present in the tissue infiltrate in all of the cases. The percentage of eosinophils was as follows: 0.1 to 4.9 in 4 cases, 10 to 19.9 in 2 cases, 20 to 29.9 in 1 case, and more than 60 in 2 cases. In 4 of the 9 cases there was a predominance of bilobed cells. In just 1 case were trilobar eosinophils present. In 3 of the cases there were almost twice as many eosinophils in the tissue infiltrate as there were in the blood.

We had an opportunity to count the cells in the vesicles in 3 of the cases. Vesicles were observed in more cases than these 3, but the condition of the cells in the vesicles was such that a differential count was impossible. In the 3 cases studied, the bilobed eosinophils predominated and the percentage of eosinophils corresponded roughly to that of the eosinophils in the tissue infiltrate. In 1 case the eosinophils had more than two lobes to their nuclei.

PEMPHIGUS VEGETANS

We were able to find just 3 cases in which we felt an accurate eosinophil count could be made. A differential blood count was made in 2 of the 3 cases. In these 2 cases the percentage of eosinophils in the blood was 13 and 14 respectively.

Eosinophils were present in the tissue infiltrate in each case. The percentage of eosinophils in the tissue infiltrate in these cases was 1.5, 5 and 11.5 respectively. In all cases this differential count was made on the cells in the cutis. The eosinophils would have been much more numerous had the count been made on some of the microabscesses in the epidermis, in which eosinophils predominate. Bilobed eosinophils predominated in 1 case; monolobed eosinophils predominated in the other 2 cases.

SUMMARY AND CONCLUSIONS

Eosinophils undoubtedly are formed in the bone marrow and enter the circulation as mature cells; however, there is good evidence that eosinophils can be formed *in loco*. This does not imply that all tissue eosinophils are of local origin. Eosinophils possess positive chemotaxis, and they are definitely phagocytic. Patients with a high percentage of eosinophils in the blood are more likely to have a local (tissue) eosinophilia after the injection of a foreign protein than are those with a normal or low percentage of eosinophils in the blood. In cases of Vidal's lichen it is unusual to observe a high percentage of eosinophils in the blood or to find eosinophils in the tissue infiltrate. Atopic dermatitis and, to a lesser extent, exudative neurodermatitis tend to produce an increase in the percentage of eosinophils in the blood as well as a considerable number of eosinophils in the tissue infiltrate. In all cases of exudative neurodermatitis, binuclear eosinophils, predominated. Eosinophils occur in the cutis in dermatitis herpetiformis and pemphigus vegetans, as well as in the bullae and abscesses in the epidermis. Binuclear eosinophils usually predominate over mononuclear eosinophils in the tissue infiltrate in cases of localized neurodermatitis, exudative neurodermatitis, atopic dermatitis or dermatitis herpetiformis.

SULFONAMIDE COMPOUNDS IN TREATMENT OF ERYSIPELOTHRIX RHUSIOPATHIAE INFECTIONS

EFFECTIVENESS OF SULFANILAMIDE, SULFAPYRIDINE, SULFATHIAZOLE AND SULFADIAZINE AGAINST EXPERIMENTAL INFECTION IN THE MOUSE AND AGAINST ERYSIPELOID OF ROSENBACH IN MAN

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This study has two purposes: The first is to report the results of determinations of the therapeutic effect of sulfanilamide, sulfapyridine, sulfathiazole and sulfadiazine in mice inoculated with Erysipelothrix rhusiopathiae. These drugs were separately employed after the animals were inoculated with the amount of a culture of the organism that normally killed in about four days. The effect of these drugs in conjunction with subcutaneous doses of immune serum was also studied. The second purpose is to discuss the effects of the sulfonamide compounds in the treatment of the infection caused in man by Ery. rhusiopathiae, erysipeloid of Rosenbach.

SULFONAMIDE COMPOUNDS IN TREATMENT OF MICE

Method of Study.—A virulent strain of Ery. rhusiopathiae was obtained from swine skin, the site of "diamond" skin disease [1] (a mild form of swine erysipelas [2]). A section of skin about 3 mm. square was excised and minced in sterile isotonic solution of sodium chloride. Three-tenths to 0.5 cc. of this solution was injected intraperitoneally into different mice. A few days later the sickest animal was killed. Pure culture of Ery. rhusiopathiae was obtained by culturing heart blood in heart infusion broth containing ascites fluid (10 per cent). Virulence was determined by inoculating mice intraperitoneally with varying amounts of a forty-eight hour culture. It was observed that 0.00002 cc. killed in four to five days. This amount injected intraperitoneally was used to inoculate the mice employed in the study.

A total of 44 mice, ranging in weight from 24 to 27 Gm., were used. Sulfanilamide, sulfapyridine, sulfathiazole and sulfadiazine were separately administered orally in doses of 0.2 Gm. per kilogram of body weight. This dose and method of administration were used throughout the study. A group of 4 mice were used for each compound. In one group the compound was administered twice daily for two days before inoculation and twice daily thereafter for six additional days. In another group, initial treatment was given four hours after inoculation and then treatments were given twice daily for six additional days. In addition, 16 mice were treated with sulfanilamide. The initial dose was administered four hours after inoculation, and doses were given twice daily for eight additional days. The animals that survived were observed for three weeks.

The control group comprised 15 mice inoculated with the same culture in the same dose as was employed for the treated animals.

From the Research Institute for Cutaneous Medicine.

1. (*a*) Klauder, J. V., and Harkins, M. J.: Erysipeloid in the United States, J. A. M. A. **96**:1205-1209 (April 11) 1931. This article contains results of a study of virulence of Ery. rhusiopathiae obtained from lesions of "diamond" skin disease and from other sources. (*b*) Klauder, J. V.; Righter, L., and Harkins, M. J.: A Distinctive and Severe Form of Erysipeloid Among Fish Handlers, Arch. Dermat. & Syph. **14**:662-678 (Dec.) 1926. This article contains detailed methods for identification of the organism.

2. The specimen was obtained from a condemned carcass in a Philadelphia abattoir through the courtesy of Dr. C. J. Millen, inspector in charge of the Philadelphia office of the Bureau of Animal Industry.

Results.—The results are shown in table 1. Of 44 mice treated with the different compounds given before and/or after inoculation, 34 (77.3 per cent) died. Ten of this number died more than five days after inoculation. All of the 15 mice comprising the control group died; only 1 survived the fifth day after inoculation.

Of 12 mice for which treatment was started before inoculation, 6 (50 per cent) died, whereas of 32 mice for which treatment was started after inoculation 28 (85.5 per cent) died.

COMBINED CHEMOTHERAPY AND SERUM THERAPY IN TREATMENT OF MICE

The minimum amount of immune serum that protected mice against the lethal dose of Ery. rhusiopathiae used in this study was determined. It was observed that about 25 per cent of mice which had received injections of 0.02 or 0.01 cc. of immune serum four hours after inoculation with Ery. rhusiopathiae survived,

TABLE 1.—*Therapeutic Effects of Sulfanilamide, Sulfapyridine, Sulfathiazole and Sulfadiazine in Treatment of Mice Inoculated with Ery. Rhusiopathiae* *

Compound	Dose, Gm./Kg.	No. of Mice	Deaths In Days 1	3	4	5	6	7	8	14	21	Total
Sulfanilamide	0.2 †	4	..	..	..	..	..	..	2	..	..	2
	0.2 ‡	4	..	1	..	..	..	1	1	..	..	3
	0.2 §	16	..	2	8	1	2	..	1	..	..	14
Sulfapyridine	0.2 †	4	..	..	..	1	..	..	..	..	..	1
	0.2 ‡	4	..	1	1	..	1	..	..	..	..	3
Sulfathiazole	0.2 †	4	..	..	2	..	1	..	..	..	..	3
	0.2 ‡	4	..	1	2	..	..	1	..	..	..	4
Sulfadiazine	0.2 ‡	4	..	2	2	..	..	..	..	..	..	4
Control	.....	15	..	4	4	6	..	1	..	..	..	15

* By intraperitoneal injection of 0.00002 cc. of a forty-eight hour culture in heart infusion broth containing ascites fluid (10 per cent).
† Orally twice daily for two days before inoculation and twice daily thereafter for six additional days.
‡ Orally four hours after inoculation and twice daily thereafter for six additional days.
§ Orally four hours after inoculation and twice daily thereafter for eight additional days.

whereas mice which had received injections of 0.005 or 0.001 cc. of immune serum four hours after inoculation died. These four dilutions of immune serum were employed in the following study.

A group of 4 mice received a single injection of each dilution of serum four hours after inoculation; each group was treated with one of the four compounds. Sixteen mice, therefore, were used for each compound. Treatment was started four hours after inoculation and then was given twice daily thereafter for six additional days.

The serum control group comprised 16 mice. Each of 4 mice was given an injection of one of the four dilutions of immune serum four hours after inoculation. None of the sulfonamide compounds was given to these animals.

The untreated control group comprised 10 mice inoculated with the same culture in the same dose as was employed in the other groups of mice.

Results.—The results are shown in table 2. Of the entire 64 mice treated with various dilutions of immune serum and with the various sulfonamide compounds, 54 (85 per cent) died. All of the 10 mice in the untreated control group died.

Of 32 mice treated with the various sulfonamide compounds and with 0.005 and 0.001 cc. of serum, 30 (80 per cent) died, whereas of 32 mice treated with 0.02 and 0.01 of serum, 24 (75 per cent) died. This lower percentage of deaths can be attributed to the partial protection of the lower dilution of serum which

these mice received and not to the therapeutic effect of the compounds, since 4 of 16 mice (75 per cent deaths) used in the serum control study survived.

COMMENT

Survival of 12.5 per cent of mice treated with sulfonamide compounds after inoculation (32 mice, table 1) and of 20 per cent in another group treated with the higher dilutions of serum in conjunction with sulfonamide compounds (32 mice table 2) shows a limited therapeutic effect of these compounds which is slightly enhanced when combined with serum.

Additional evidence of some therapeutic effect is the greater percentage (50 per cent) of survival of the animals treated before inoculation and the longer time of

TABLE 2.—*Therapeutic Effects of Sulfanilamide, Sulfapyridine, Sulfathiazole and Sulfadiazine in Conjunction with Subcurative Dose of Immune Serum in Treatment of Mice Inoculated with Ery. Rhusiopathiae* *

Compound †	Dose of Serum, Cc.‡	No. of Mice	Deaths In Days 1	2	3	4	5	6	7	8	10	14	Total
Sulfanilamide	0.02	4	..	..	..	..	1	1	..	..	..	..	2
	0.01	4	..	..	2	..	1	1	..	..	..	..	4
	0.005	4	..	..	..	4	..	..	..	..	..	..	4
	0.001	4	..	..	1	2	1	..	..	..	..	..	4
Sulfapyridine	0.02	4	..	..	..	..	2	..	..	..	1	..	3
	0.01	4	..	..	2	2	1	..	..	..	..	..	3
	0.005	4	..	..	..	2	1	..	..	..	..	1	4
	0.001	4	..	..	2	1	1	..	..	..	..	..	4
Sulfathiazole	0.02	4	..	..	..	..	..	1	..	1	..	..	2
	0.01	4	..	..	..	..	2	..	..	..	..	1	3
	0.005	4	..		..	..	3	..	..	..	..	..	3
	0.001	4	..	..	..	..	3	..	1	..	..	..	4
Sulfadiazine	0.02	4	..	..	..	..	2	..	..	..	..	1	3
	0.01	4	..	..	..	2	1	..	..	..	1	..	4
	0.005	4	..	..	1	3	..	..	..	..	..	..	4
	0.001	4	..	..	1	3	..	..	..	..	..	..	4
Serum only	0.02	4	..	..	..	..	..	2	1	..	..	..	3
	0.01	4	..	..	..	..	..	2	1	..	..	..	3
	0.005	4	..	..	..	..	2	2	..	..	..	..	4
	0.001	4	..	..	..	2	1	1	..	..	..	..	4
No treatment	....	10	..	2	3	3	1	..	1	..	..	..	10

* By intraperitoneal injection of 0.00002 cc. of a forty-eight hour culture in heart infusion broth containing ascites fluid (10 per cent).

† Initial dose (given orally) of 0.2 Gm. per kilogram of weight four hours after inoculation and the same amount twice daily thereafter for six additional days.

‡ A single injection given four hours after inoculation.

survival of animals treated after inoculation compared with those of the untreated control group.

These results do not compare, however, with those obtained by the therapeutic effect of sulfanilamide in treatment of experimental streptococcic or staphylococcic infection in mice or with the effect of immune serum in treatment of mice inoculated with Ery. rhusiopathiae.

Most experimental investigations of the therapeutic effect of sulfanilamide on streptococcic infection of mice has been conducted with group A streptococci. The percentage of mice treated with sulfanilamide surviving lethal doses of such organisms ranged from 37 to 100 per cent as reported by different investigators.[3] In experimental staphylococcic infection of mice for which sulfanilamide, sulfapyridine or

3. Kolmer, J. A.: Progress in Chemotherapy of Bacterial and Other Diseases, with Special Reference to the Prontosils, Sulfanilamide and Sulfapyridine, Arch. Int. Med. **65**: 671-743 (April) 1940.

sulfathiazole was employed in treatment, the percentage that survived ranged from 8 to 70 per cent as reported by different investigators.

Porter and Hale [4] studied the therapeutic effect of sulfapyridine in treatment of mice inoculated with Ery. rhusiopathiae and also with Listerella monocytogenes.[5] One cubic centimeter of a 0.5 per cent solution of sulfanilamide in a 5 per cent solution of dextrose in isotonic solution of sodium chloride was injected intraperitoneally. Two cubic centimeters of a saturated solution (about 0.1 to 0.2 per cent) of sulfapyridine was similarly injected. Initial treatment with the sulfonamide compounds was given three to four hours after inoculation with the organism, and treatment was continued every four hours for five days. Sulfanilamide and sulfapyridine had no therapeutic effect in treatment of the mice inoculated with Ery. rhusiopathiae. Indeed, the treated animals died quicker than the controls. A limited therapeutic effect was observed in mice inoculated with L. monocytogenes. Fourteen of 60 mice treated with sulfanilamide and 2 of 20 mice treated with sulfapyridine died, whereas 77 of 80 mice used as controls died.

SULFONAMIDE COMPOUNDS IN TREATMENT OF ERYSIPELOID INFECTION IN HUMAN BEINGS

The limited therapeutic value of the sulfonamide compounds against the infection in mice does not suggest their efficacy in treatment of the infection in human beings. In our experience no striking results were obtained with sulfonamide compounds in treatment of erysipeloid. In the following case a patient received 4 Gm. of sulfanilamide for ten consecutive days, without effect on the erysipeloid.

A white man who worked in an abattoir scratched the right palm on a splinter of bone when handling the carcass of a swine. The injury occurred on January 22. The following day the entire palm was painful, red and edematous. Cellulitis was diagnosed, and 4 Gm. of sulfanilamide daily was administered starting on January 24. Inflammation extended to the dorsa; lymphangitis appeared, and the patient had fever. He was then hospitalized.

In addition to local treatment, 4 Gm. of sulfanilamide was administered daily throughout hospitalization until the patient was discharged, on February 3. At the time of his discharge the cellulitis disappeared. In the center of the palm there was a bluish red patch of erythema, and the thumb was bluish red, tense and swollen. Erysipeloid of Rosenbach was then diagnosed. Constant wet dressing of 12 per cent ichthammol in alcohol was applied and a splint placed on the hand. The patient was discharged as cured on February 14.

The sulfonamide compounds have been reported to have been apparently successfully employed in treatment of erysipeloid. In each of such reports [6] one of the

4. Porter, J. R., and Hale, W. M.: Effect of Sulfanilamide and Sulfapyridine on Experimental Infections with Listerella and Erysipelothrix in Mice, Proc. Soc. Exper. Biol. & Med. **42**:47-50, 1939.

5. L. monocytogenes and Ery. rhusiopathiae are similar morphologically and culturally. One difference, however is that L. monocytogenes is motile whereas Ery. rhusiopathiae is nonmotile. Both organisms are the cause of widespread infection in animals.

6. (*a*) Schoch, A. G., and Shelmire, B.: Erysipeloid of Rosenbach Successfully Treated with Sulfanilamide, Arch. Dermat. & Syph. **41**:570-571 (March) 1940. (*b*) Durand, P.: Un érysipéloïde anormalement situé (quelques remarques à ce sujet), Presse méd. **48**:355-356, 1940. (*c*) Arguelles Casals, D.: La sulfanilamida y sus derivados en el tratamiento del erisipeloide de Baker Rosenbach; a propósito de un caso, Rev. de med. trop. y parasitol., bacteriol., clín. y lab. **7**:72-73, 1941. (*d*) Eckstein, A. W.: Erysipeloid: Report of Case Treated with X-Ray and Sulfanilamide, Rhode Island M. J. **24**:41-45, 1941. (*e*) Peyer, G.: Ueber die Behandlung des Schweinerotlaufs beim Menschen (Erysipeloid) mit Ciba 3714, Schweiz. med. Wchnschr. **71**:159, 1941. (*f*) Grinnan, R. B., and Martin, W. B.: Erysipeloid: Report of a Case, Arch. Dermat. & Syph. **41**:1037-1043 (June) 1940. (*g*) Combes, F. C., and Canizares, O.: Sulfanilamide and Allied Compounds: Their Value and Limitations in Dermatology, ibid. **44**:236-247 (Aug.) 1941. (*h*) Kulchar, G. V., and Rosenberg, E.: Sulfathiazole in the Treatment of Erysipeloid, ibid. **43**:846-847 (May) 1941.

compounds was used in treatment of either one or a few patients. The course of erysipeloid is variable. Elsewhere [7] one of us (J. V. K.) reported 100 cases of erysipeloid with treatment by various methods and included in the report the duration of the disease from onset to recovery. The following statement was made: "Indeed it is difficult to evaluate different methods of treatment since in many cases erysipeloid apparently runs a self-limited course and splinting the hand may be the only required treatment."

Calloman [8] and Pawlowski [9] stated the opinion that evaluation of the results of treatment of erysipeloid is difficult since in a large proportion of cases the disease tends to eventual recovery without any treatment. Indeed, Calloman commented on the small number of cases which authors deemed to be sufficient for evaluation of newly recommended remedies.

The sensitizing capabilities of the sulfonamide compounds should alone restrain their use in treatment of erysipeloid, which usually pursues a self-limited course.

In the patient reported by Klauder, Kramer and Nicholas [10] with blood stream infection with Ery. rhusiopathiae, 15 Gm. of sulfathiazole given in four days was without beneficial effect. In Russell and Lamb's [11] patient with Ery. rhusiopathiae septicemia, sulfanilamide (dose not stated) was without avail.

Antiserum remains the treatment of choice for patients with severe forms of erysipeloid and for patients with the septicemic form of infection. Klauder and Harkins [12a] observed that antiserum in doses of 0.2 cc. protected mice against one thousand times the fatal dose of Ery. rhusiopathiae.

One of us (J. V. K.), however, reported on a patient with a generalized cutaneous form of infection with polyarthritis (culture of the blood gave negative results).[12] Large repeated doses of antiserum (given late in the infection) failed to cure; disappearance of symptoms after injection was only temporary. Calloman [8] and other writers have reported failure from serum therapy.[13] In such cases, serum therapy combined with one of the sulfonamide compounds would be indicated.

SUMMARY AND CONCLUSIONS

Sulfanilamide, sulfapyidine, sulfathiazole and sulfadiazine were separately administered to mice orally in doses of 0.2 Gm. per kilogram of body weight. To some the compounds were administered twice daily for two days before inoculation with a virulent strain of Ery. rhusiopathiae and twice daily thereafter for six additional days. For others initial treatment was four hours after inoculation and then twice daily for six additional days; in still others, for eight additional days.

7. Klauder, J. V.: Erysipeloid as an Occupational Disease, J. A. M. A. **111**:1345-1348 (Oct. 8) 1938.

8. Calloman, F.: Pseudoerysipel Erysipeloid, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1929, vol. 9, pt. 1.

9. Pawlowski, E.: Die Klinik und Therapie des Erysipeloids, Deutsche med. Wchnschr. **58**:1366, 1932.

10. Klauder, J. V.; Kramer, D. W., and Nicholas, L. N.: Erysipelothrix Rhusiopathiae Septicemia: Diagnosis and Treatment; Report of Fatal Case of Erysipeloid, J. A. M. A. **122**:938-943 (July 31) 1943.

11. Russell, W. O., and Lamb, M. E.: Erysipelothrix Endocarditis: A Complication of Erysipeloid, J. A. M. A. **114**:1045-1050 (March 23) 1940.

12. Klauder, J. V.: Generalisiertes Erysipeloid: Bericht über einen 20 Monate dauernden Fall mit Sektionsbefund, Dermat. Wchnschr. **98**:613-619, 1934.

13. The studies of Kurtzahn (Erfahrungen an 200 Erysipeloidfällen, Med. Welt **2**:97, 1928) suggest that the period of the disease in which serum is first used is a determining factor of its efficacy or failure. His observations suggest that results of serum therapy are in proportion to the promptness of its use.

Survival of 12.5 per cent of mice treated with a sulfonamide compound after inoculation shows a limited therapeutic effect of these compounds, which is slightly enhanced when they are employed in conjunction with subcurative injections of immune serum.

Sulfonamide compounds were ineffective in treatment of patients with erysipeloid and of 1 patient with the septicemic form of infection with Ery. rhusiopathiae. Antiserum remains the treatment of choice for human subjects with severe forms of infection. Combined therapy with serum and a sulfonamide compound is indicated for patients whose infection is of long duration.

The incidence of sensitization to sulfonamide compounds is sufficiently great to restrain their use in treatment of erysipeloid, which is usually self limited.

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NUTRITIONAL DERMATOSES IN THE RAT

X. A COMPARISON OF DISSEMINATED NEURODERMATITIS AND EXPERIMENTAL MAGNESIUM DEFICIENCY

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When young rats are fed an otherwise adequate diet which contains insufficient magnesium there develops a disease characterized by hyperexcitability, tonic-clonic convulsive seizures, nephritis, hepatitis, vasodilatation, intense generalized erythema, edema of the skin, erythema multiforme, dermatitis, ulcers, hyperflexibility and hyperextensibility of the joints, edema of the dependent parts and finally nutritive failure and death.[1] Magnesium deficiency in calves results in the deposition of calcium salts in the yellow elastic fibers of the endocardium, of the aorta, jugular vein and larger arteries, of the surfaces of the diaphragm and of the trabeculae of the spleen.[2] Clinicians generally have lacked interest in magnesium deficiency and have neglected to explore the possibilities of its clinical significance. The clinical implications suggested by the experimental syndrome include tetany,[1] epilepsy,[3] arteriosclerosis,[2] nephrosis[4] and disseminated neurodermatitis.[5] In this communication disseminated neurodermatitis is compared with experimental magnesium deficiency and the claim for their similarity is evaluated.

I. A COMPARISON OF THE GROSS SIGNS AND THE SYMPTOMS OF DISSEMINATED NEURODERMATITIS IN MAN AND OF MAGNESIUM DEFICIENCY IN THE RAT

The well known signs of disseminated neurodermatitis (atopic dermatitis) need not be recounted in detail. The following brief description is recorded as a basis for a comparison with the experimental disease: Disseminated neurodermatitis is a disease of infants, children and young adults.[6] It is of long duration, and during its protracted course there are remissions and recurrences. The lesion consists of symmetrically distributed plaques of chronic inflammation of the skin in which there are at various times erythema, edema, papules, vesicles, scaling, crusting, hyperpigmentation, thickening and exaggeration of the folds of the skin. Pruritus is usually severe, and excoriations are common. Often there are superimposed signs of inflammation due to complicating pyococcic infections and dermatitis of external contact origin. The sites of predilection[7] in order of frequency of involve-

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From the Department of Dermatology, Johns Hopkins University School of Medicine, and the Department of Biochemistry, Johns Hopkins University School of Hygiene and Public Health.

1. (*a*) McCollum, E. V., and Orent, E. R.: Effects in the Rat of Deprivation of Magnesium, J. Biol. Chem. **92**:xxx, 1931. (*b*) Kruse, H.; Orent, E. R., and McCollum, E. V.: Studies on Magnesium Deficiency in Animals: I. Symptomatology Resulting from Magnesium Deprivation, ibid. **96**:519 (May) 1932. (*c*) Tufts, E. V., and Greenberg, D. M.: Nature of Magnesium Tetany, Am. J. Physiol. **121**:416 (Feb.) 1938. (*d*) Watchorn, E., and McCance, R. A.: CLXII. Subacute Magnesium Deficiency in Rats, Biochem. J. **31**:1379 (Aug.) 1937. (*e*) Schrader, G. A.; Prickett, C. O., and Salmon, W. D.: Symptomatology and Pathology of Potassium and Magnesium Deficiencies in the Rat, J. Nutrition **14**:85 (July) 1937. (*f*) Sullivan, M., and Evans, V. J.: Nutritional Dermatoses in the Rat: IX. Evaluation of the Interrelationship of Magnesium Deficiency and Deficiencies of the Vitamin B Complex, to be published. (*g*) Kruse, H. D.; Schmidt, M. M., and McCollum, E. V.: Studies on Magnesium Deficiency in Animals: V. Changes in the Mineral Metabolism of Animals Following Magnesium Deprivation, J. Biol. Chem. **106**:553 (Sept.) 1932. (*h*) Orent, E. R.; Kruse, H. D., and McCollum, E. V.: Studies on Magnesium Deficiency in Animals: VI. Blood Changes in the Bone with Associated Blood Changes Resulting from Magnesium Deprivation, ibid. **106**:573 (Sept.) 1934.

2. Moore, L. A.; Hallman, E. T., and Sholl, L. B.: Cardiovascular and Other Lesions in Calves Fed Diets Low in Magnesium, Arch. Path. **26**:820 (Oct.) 1938.

3. Hirschfelder, A. D., and Haury, V. G.: Variations in Plasma Magnesium and Potassium in Epilepsy, Proc. Soc. Exper. Biol. & Med. **33**:40 (Oct.) 1935.

4. Greenberg, D. M.; Lucia, S. P., and Tufts, E. V.: The Effects of Magnesium Deprivation on Renal Function, Am. J. Physiol. **121**:424 (Feb.) 1938.

5. (*a*) Engman, M. F., and MacCardle, R. C.: A Histochemical Study of Neurodermatitis, Arch. Dermat. & Syph. **42**:109 (July) 1940. (*b*) MacCardle, R. C.; Engman, M. F., and Engman, M. F., Jr.: Histology of Neurodermatitis, ibid. **44**:161 (Aug.) 1941; (*c*) Spectrographic Analysis of Neurodermatitic Lesions, ibid. **44**:429 (Sept.) 1941; (*d*) Mineral Changes in Neurodermatitis Revealed by Microincineration, ibid. **47**:335 (March) 1942.

6. Sulzberger, M. B.: Dermatologic Allergy, Springfield, Ill., Charles C Thomas, Publisher, 1940, p. 162.

7. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 10, St. Louis, C. V. Mosby Company, 1939, p. 235. Greenhill, M. H., and Finesinger, J. E.: Neurotic Symptoms and Emotional Factors in Atopic Dermatitis, Arch. Dermat. & Syph. **46**:187 (Aug.) 1943.

ment are the cubital and popliteal areas, the sides and back of the neck, the face, the head, the axillas, the shoulders and the thorax. The lower part of the trunk and lower extremities, exclusive of the popliteal areas, sometimes remain free of the eruption. Changes in personality [7] have been reported, prolonged discomfort, pain and embarrassment likely account for such

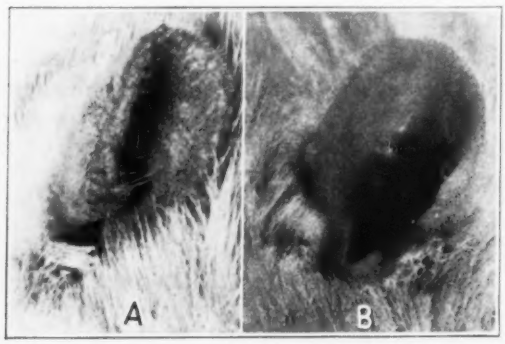

Fig. 1.—The first cutaneous sites of involvement are the conchae of the ears and the retroauricular regions. The erythema spreads rapidly and involves all of the ear (*A*). Edema accompanies the erythematous stage and persists after the erythema subsides. Note the increased thickness of the ear. *B* shows a normal ear for comparison.

changes.[8a] Cataract [9] and keratoconus [10] have been noted as complications. Nephritis occasionally occurs, especially when there is extensive complicating pyoderma.

The experimental magnesium deficiency syndrome can be produced in rats of any age. In young rats the onset of the signs occurs three to four days after the deficient ration is fed; in older rats the onset is delayed for several days to several weeks. The first sign is hyperirritability. The first cutaneous signs are erythema and edema. The conchae of the ears and the retroauricular regions usually are the sites of initial implication; swelling and redness spread to the tips of the ears (fig. 1 *A*), and shortly thereafter the trunk and extremities are implicated by diffuse erythema or by multiformed erythematous plaques (fig. 2). Coincident with the signs of vasodilatation, tonic-clonic convulsive seizures spontaneously occur or may be induced by noise and by handling (fig. 13). There is tachycardia [1b] in the hyperemic stage. This is followed by a period in which there are bradycardia and arrhythmia. After variable periods the erythema subsides, and there is pallor of the skin and visible mucous membranes. Edema of the skin and the subcutanea persists; it is most extensive in the dependent parts. The skin loses its resiliency; when the skin of the back is grasped between the forefinger and the thumb, lifted and then released, the folded skin slowly returns to its position (fig. 3). In some rats after one or two attacks of generalized or of multiformed plaques of erythema there are no further gross cutaneous signs. In other animals there are round and oval plaques of nonpruritic, scaly and occasionally eczematous and crusted dermatitis on the snout, neck, tail and trunk (fig. 4). The plaques persist throughout the

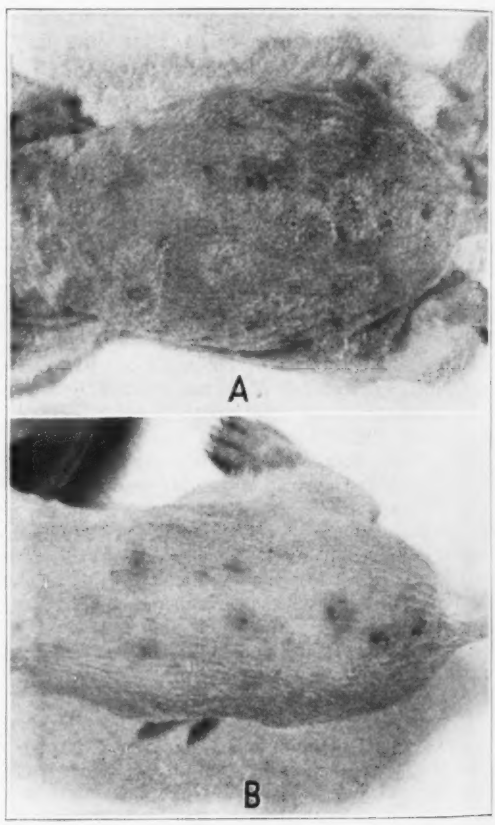

Fig. 2.—Two examples of multiformed erythematous plaques involving the trunk.

life of the animals, and in some animals there are progressive changes, particularly in the tail, consisting of ulceration and gangrene (fig. 5). The ears remain thickened, and on the margins there are crusts. Ulcers frequently involve the edematous plantae (fig. 6 *B*). The flexural surfaces are not involved. In the late stages of the dis-

8. Wise, F., and Sulzberger, M. B.: (*a*) Editorial comment on abstract of reference 7, in Year Book of Dermatology and Syphilology, Chicago, Year Book Publishers, Inc., 1942, p. 98; (*b*) Editorial comment on abstract of reference 5a, ibid., p. 101.

9. Brunsting, L. A.: Atopic Dermatitis (Disseminated Neurodermatitis) in Young Adults, Arch. Dermat. & Syph. **34**:935 (Dec.) 1936.

10. Bereston, E. S., and Baer, R. L.: Keratoconus Associated with Atopic Dermatitis, Arch. Dermat. & Syph. **46**:358 (Sept.) 1942.

ease nutritive failure sets in. There is hematuria. The animals assume a negativistic attitude and are reluctant to be handled. There are nonspecific signs of deficiency and malnutrition consisting of alopecia, generalized brown crusting, lack of hygiene, loss of weight and emaciation.

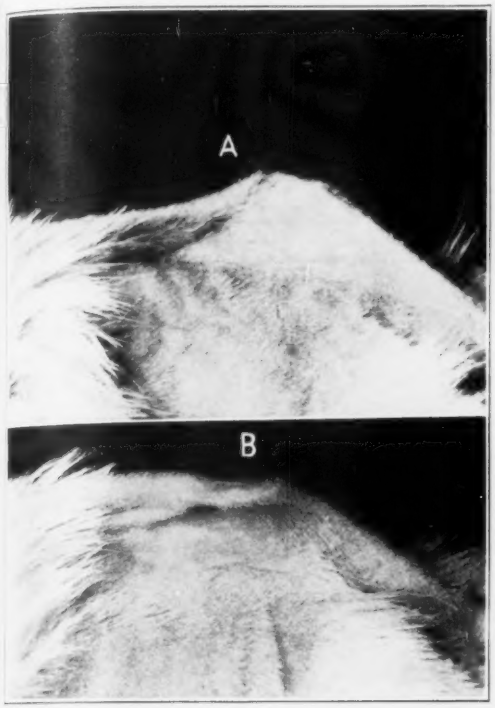

Fig. 3.—The edematous skin loses its resiliency. When it is grasped between the forefinger and the thumb, lifted (*A*) and then released (*B*), the folded skin returns slowly to its position.

Fig. 4.—Scaly, eczematous and crusted plaques of dermatitis involve the various areas of the skin in the late stage of the disease. This photograph shows scaly dermatitis on the back of the neck.

Cataracts were not observed in 200 animals in our experiments, and other observers have not reported cataract as a complication. Gingival hypertrophy was observed by Klein, Orent and McCollum,[11] but it was not reproduced in these experiments. Hepatitis occurred in a high percentage of the animals. In some rats there were sclerotic changes in the large vessels, and enlargement of the parathyroids was observed in a few animals that had survived for several months.

Fig. 5.—Gangrene of the tail is a late complication.

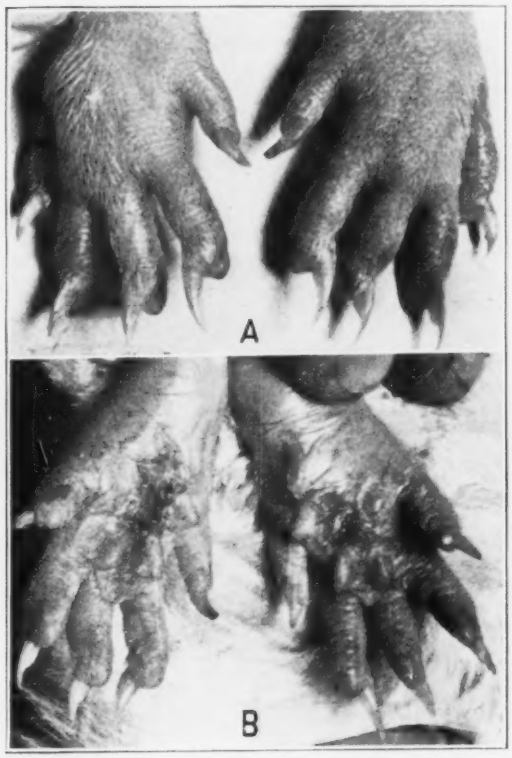

Fig. 6.—*A* shows extensive edema and erythema of the paws and *B*, ulcers of the paws.

11. Klein, H.; Orent, E., and McCollum, E. V.: The Effects of Magnesium Deficiency on the Teeth and Their Supporting Structures in Rats, Am. J. Physiol. **112**:256 (June) 1935.

II. COMPARISON OF MICROSCOPIC CHANGES IN DISSEMINATED NEURODERMATITIS IN MAN AND MAGNESIUM DEFICIENCY IN THE RAT

Disseminated Neurodermatitis	Experimental Magnesium Deficiency
Hyperkeratosis is a common finding. The corneum is eight to ten times thicker than the normal corneum. There are occasionally small areas of parakeratosis.	Hyperkeratosis is not a constant finding. When it occurs it is less extensive than that observed in disseminated neurodermatitis (figs. 7 and 9). The corneum is rarely more than four or five times thicker than the normal corneum. Parakeratosis occurs especially in the vicinity of ulcers (fig. 8).

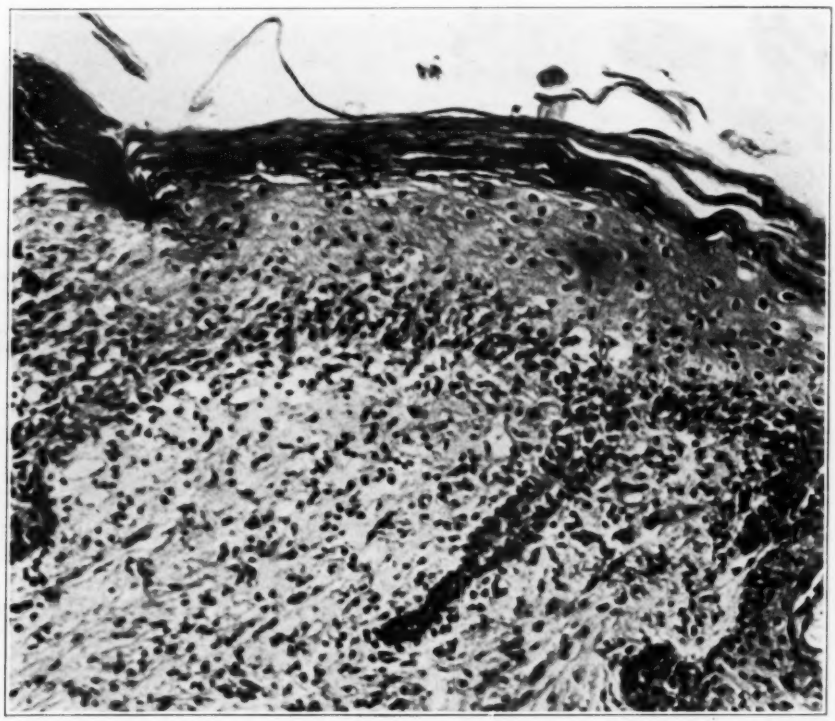

Fig. 7.—Tail (× 240), showing moderate hyperkeratosis, acanthosis and vacuolation of some of the epidermal cells which contain shrunken and deeply staining nuclei. There is diffuse cellular infiltration in the cutis and beginning encroachment on the epidermis by exudative cells.

In the hyperkeratotic lamellae there are keratin deposits which are stained intensely with ponceau xylidine of Masson's stain but which fail to take the hematoxylin and eosin stain.	The keratin deposits described by MacCardle and associates are not present. Keratohyalin granules are occasionally extruded into the corneum, and these granules stain with hematoxylin and eosin.
The intercellular fibrils are thicker than normal and are heavily stained with ponceau xylidine under areas of hyperkeratosis.	There are a few scattered areas in the epidermis where the intercellular canals are sufficiently dilated to permit study of the intercellular fibrils. It is difficult to estimate whether the fibrils are increased in thickness; they are not heavily stained with ponceau xylidine.

Neurodermatitis (Continued)	Magnesium Deficiency (Continued)
The nuclei of all spinous cells are larger than those of normal spinous cells, and they are much less intensely colored with acid fuchsin. The chromatin is thinned, and the nucleoli are more numerous in the spinous cells nearest the basal cells.	The nuclei of the spinous cells are not larger than normal spinous cells. Comparative measurements utilizing sections from deficient rats and their litter mate controls show that the nuclei of the spinous cells are not enlarged or are only slightly enlarged in certain stages. The increase in size never exceeds the ratio of 1.5 : 1. Some of the nuclei are less intensely stained with acid fuchsin. In many cases, where there is vacuolation of the cytoplasm and the nuclei are shrunken and pyknotic and deeply stained (fig. 7). Nucleoli are not more numerous in lower layers of the spinous cells.

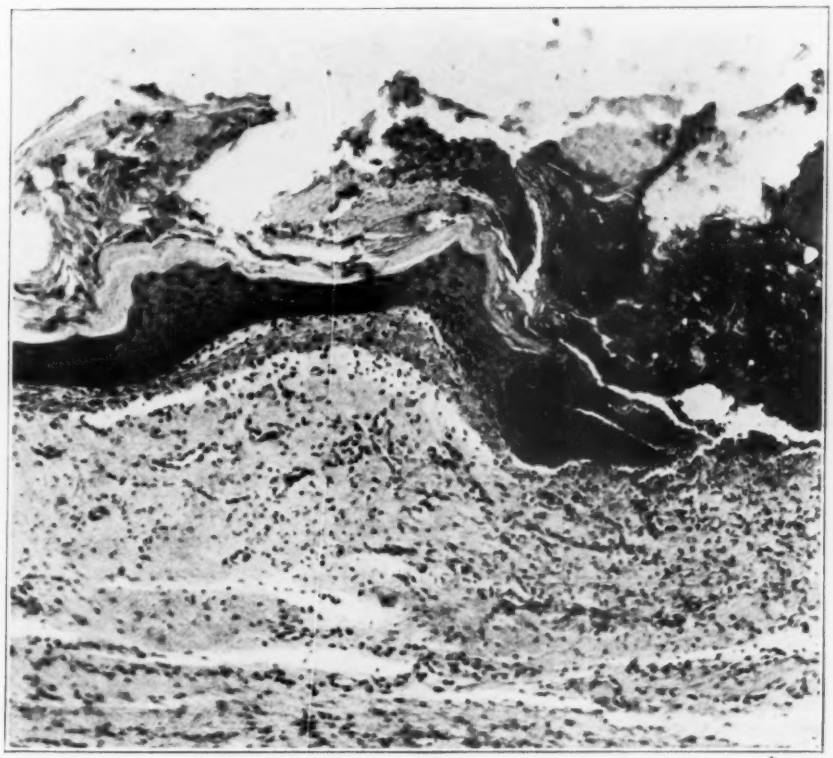

Fig. 8.—Planta (× 180). In the vicinity of ulcers there are parakeratosis and thick crusts. Note the diffuse cellular infiltration and edema in the lower part of the cutis.

In preparations stained with hematoxylin and eosin the nucleoli of spinous cells are all faintly stained with hematoxylin.	In preparations stained with hematoxylin and eosin only one nucleolus of a spinous cell is heavily stained and the remaining ones are faintly colored.
The chromatin is thinned and the nucleoli are more numerous in the spinous cells nearest the basal layer.	In areas of acanthosis, where there are sufficient epidermal layers to make possible a comparison, the nucleoli are more numerous in the spinous cells nearest the basal cells.
Usually all of the nucleoli are stained with ponceau xylidine. In hematoxylin and eosin stained preparations the nucleoli of spinous cells are all faintly stained with hematoxylin.	As in normal skin, usually one nucleolus is heavily stained and the remaining ones are faintly colored.

Neurodermatitis (Continued)

The basal layer is sometimes apparently invaded by a large number of clear cells that resemble monocytes. These cells are of a different type than those seen in normal skin. They are larger; there are no vacuoles or cytoplasmic strands, and the faintly stained nucleus is at least twice as large as normal. The rounded portions of the cytosomes protrude into the cutis, while relatively thin cytoplasmic "pseudopodia" of their epidermal surfaces extend into the interspaces between the heavily stained basal cells.

In active lesions in which the epidermis is thinned and broken over the edematous surface of an expanded papilla, the collagenic fibers are thick and tightly bound around the rete pegs but thinner and more loosely bound at the epidermal surfaces of the papillae.

In the dermal papillae there are usually many wandering isolated blood cells and connective tissue cells. In a few instances the wandering monocytes contain granules of a greenish brown pigment which may be shown by incineration to contain iron. In the deeper part of the cutis there are a few chromatophores.

Magnesium Deficiency (Continued)

"Clear cells" are occasionally seen in the basal layer. In some cases there is invasion of the epidermis by exudative cells from the cutis, after which there is disintegration of the epidermal cells (fig. 10 *A*) resulting in superficial ulceration and crust formation. Bullae (fig. 10 *B*) occasionally arise on the mucous membranes.

Fig. 9.—Ear (× 60), showing extensive hyperemia, dense cellular infiltration in the cutis and ulcer (lower right). Note the slight amount of scaling and epidermal change in contrast to the extensive involvement of the cutis.

The first detectable microscopic changes occur in the lower part of the cutis and in the subcutanea and consist of edema and hyperemia (fig. 11). There is dissociation of the connective tissue in the lower half of the cutis. Later there is a diffuse cellular infiltration which at first is sparse and later is dense. The edema spreads to involve the upper half of the cutis, and the connective tissue fibers are no longer closely apposed. During and for several months after the initial signs of cutaneous alteration the cutis is thicker than normal. The increased thickness probably depends on the amount of edema present rather than on an increase in the amount of connective tissue. The collagenic fibers are not thick and bound tightly around the rete pegs.

There is a diffuse cellular infiltration which is more extensive as the lesion develops. The type of cells varies considerably at different stages. During certain periods the predominating cell is a small mononuclear cell with nongranular cytoplasm that stains diffusely with eosin. Chromatophores are seen only in the upper part of the cutis.

Neurodermatitis (Continued)

There is always dilatation of the blood vessels, and there is mild perivascular infiltration. However, beneath the most acanthotic epidermis perivascular infiltration is seldom more evident than in some areas of apparently normal skin. Beneath areas where the epidermis is breaking down over an edematous papilla there is extensive perivascular infiltration.

Magnesium Deficiency (Continued)

Often after the acute stage dilatation of the vessels persists. Perivascular cellular infiltration is usually not evident, perhaps because of the diffuse distribution of cellular infiltration in the cutis (fig. 9).

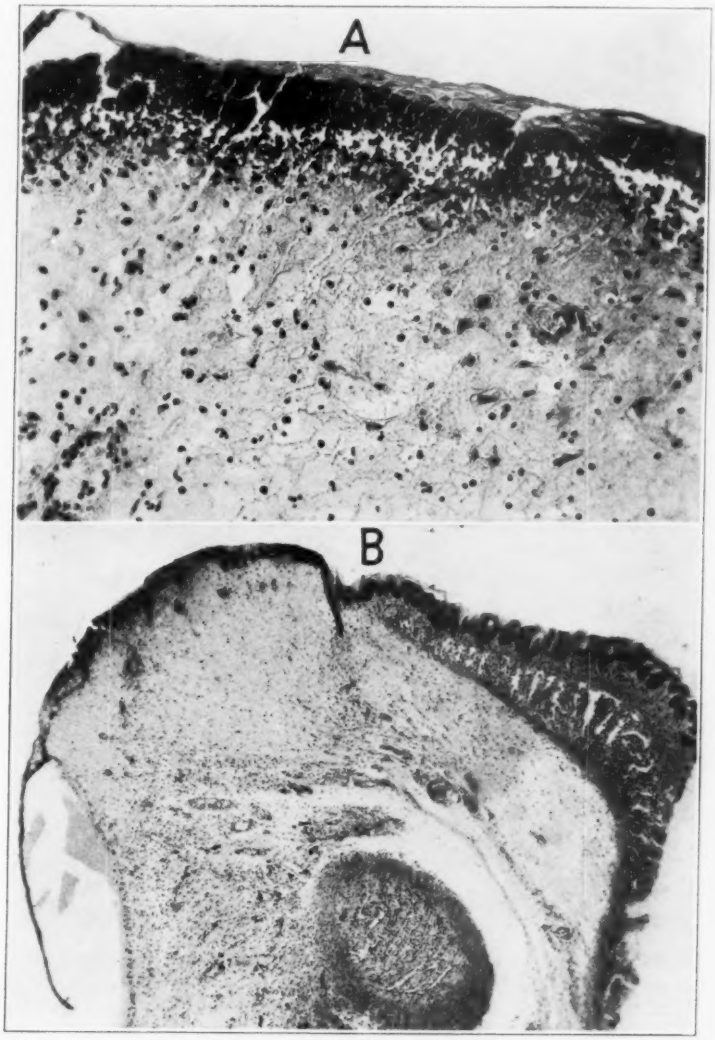

Fig. 10.—*A*, penis (× 200) showing encroachment of exudative cells on and disintegration of the epidermis. Note the edema, hyperemia and diffuse cellular infiltration in the cutis. *B*, penis (× 30) showing extensive edema in the cutis and a bulla (lower left corner).

In the kidneys there are extensive degeneration in the tubules and glomeruli and deposition of calcareous material in the areas of degeneration (fig. 12). In the livers there are extensive changes consisting of dilatation of the vessels, hyperemia and perivascular edema in the early stage and various degrees of degeneration of the liver cells in the later stages.

III. COMPARISON OF THE CHEMICAL DATA FOR HUMAN SUBJECTS WITH DISSEMINATED NEURODERMATITIS AND WITH EXPERIMENTAL MAGNESIUM DEFICIENCY

Disseminated Neurodermatitis	Experimental Magnesium Deficiency
The diet contains adequate natural sources of magnesium.[5]	The diet is deficient in magnesium.

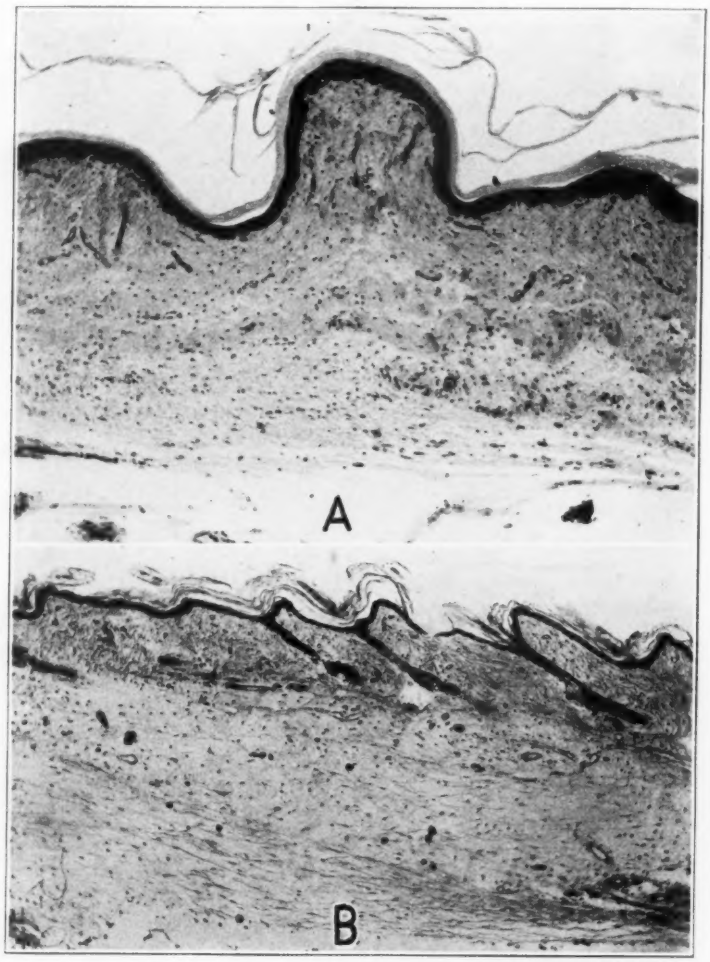

Fig. 11.—*A* and *B*, dorsa of paw and planta (× 60). These demonstrate the initial sign of cutaneous alteration, which consists of edema and hyperemia in the lower part of the cutis. The epidermal changes are secondary.

The plasma magnesium level is within normal limits.	In the first phase of the deficiency the plasma magnesium level undergoes a sharp drop and then rises to a peak shortly after the onset of hyperexcitability. It falls off again during the second phase at a relatively slow rate.[1h]
Urinary and fecal excretion of magnesium are within normal limits.[5]	Magnesium excretion is diminished throughout the entire survival period. The intestine retains magnesium more than the kidneys during the first period. There is a diminished output of magnesium in the urine, but the retention largely is due to its diminished output in the feces.[1g]

Neurodermatitis (Continued)	Magnesium Deficiency (Continued)
There is a decrease or an absence of magnesium in the skin.[5]	In acute magnesium deficiency of rats the magnesium content of the skin approximately equals the magnesium content of the skin of normal littermate controls.[1e] In chronic magnesium deficiency there is slight if any significant decrease in magnesium.

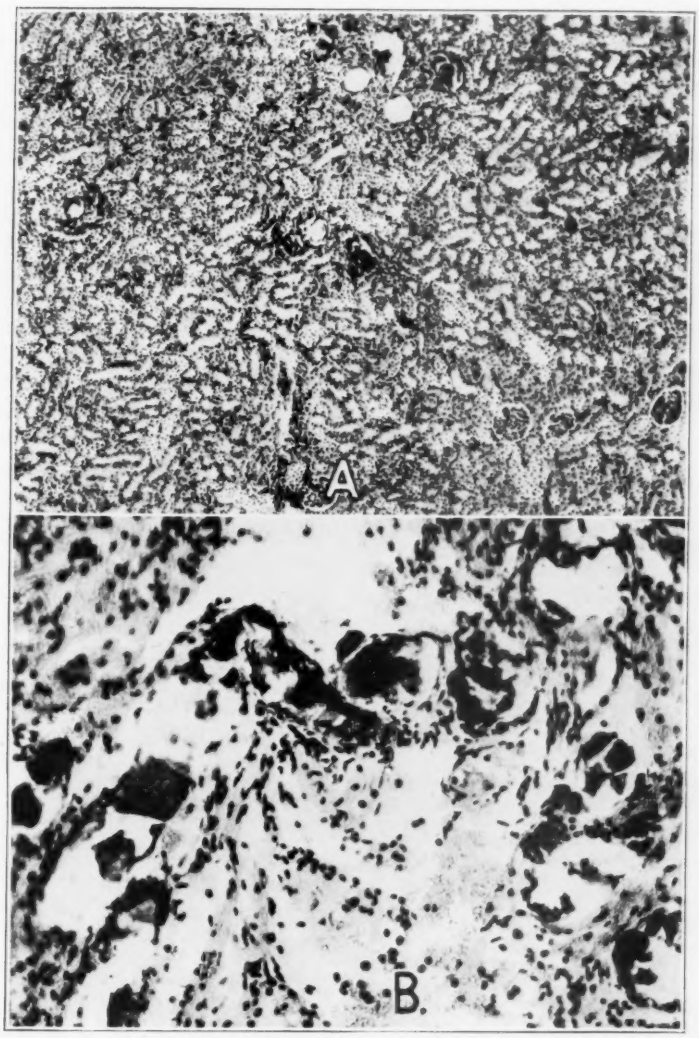

Fig. 12.—*A* and *B* are photomicrgoraphs of a kidney (× 60 and × 220), showing tubular and glomerular changes and calcareous deposits in the areas of degeneration.

The calcium content of the skin is decreased.	There is no decrease in the calcium content of the skin.[1]
There is no disturbance of serum calcium.	During the early stage of the deficiency the course of calcium metabolism is that of progressively increasing retention; thereafter there is progressively increasing elimination.[1g]

It is not possible strictly to compare, symptom for symptom and sign for sign, a disease of an animal and one of man; insofar as it is possible to make a comparison, the gross signs of the two diseases under consideration have little in common. However, histologic changes are more appropriate for comparison, as microscopic changes in similar tissues may show identical alterations or abnormalities and thereby establish a claim for analogy. The tabulation in section II is a comparison of the microscopic changes of the skin in disseminated neurodermatitis in man

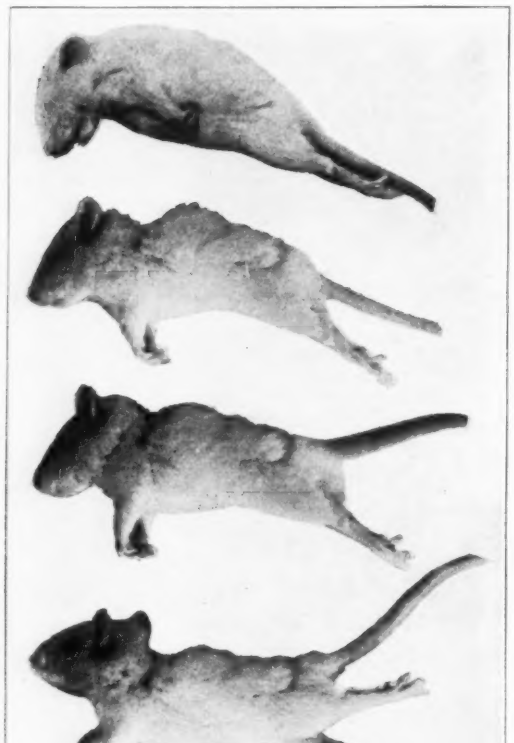

Fig. 13.—The stages of the convulsive seizures. The animal races widely around the cage in great confusion. It falls on its side and is extremely spastic in the first stage of the seizure; the eyes are closed tightly; the extremities are hyperextended stiffly for several seconds, after which the eyelids gradually open, the animal relaxes and the extremities are flexed rapidly. This stage is usually followed by a stage in which the animal is again rigid and opisthotonic. The animal then lies in a semisomnolent state; it is listless, flaccid and clumsy for a few minutes before it recovers or dies.

described by MacCardle, Engman and Engman [5] and the microscopic changes observed by us in magnesium deficiency of the rat.

An analysis of the comparative microscopic changes discloses a few similarities at some stages but also sufficient differences to cast doubt on the identity of the diseases. Chemical data also are suitable for comparison. In tabular form in section III are summarized important chemical characteristics of human experimental diseases.

IV. OTHER CRITERIA FOR COMPARISON

a. Allergy.—That disseminated neurodermatitis is in part due to, or at least associated with, an abnormal allergic state is an established fact, which probably would not be denied by proponents of various other theories concerning its cause. Failure of therapy based on elimination of offending atopens and repeated unsuccessful attempts at desensitization have provoked some dermatologists to discredit allergy in connection with disseminated neurodermatitis, but authoritative evidence [8b] is in favor of regarding the phenomenon of hypersensitization as an important factor in the disease. The rat is an unsuitable beast in which to study the phenomenon of hypersensitization. We have been unsuccessful in numerous attempts to produce cutaneous hypersensitization in normal rats and in rats suffering with various nutritional dermatoses. Under certain experimental circumstances it is possible to produce evidence of cutaneous hypersensitivity in rats.[12] If it were possible to produce cutaneous hypersensitivity in rats with magnesium deficiency, a point in favor of analogy would be established. The histologic changes of edema and hyperemia suggest that this may be in the realm of reasonable possibilities, inasmuch as there is at some stages an obvious resemblance to another allergic phenomenon, namely, urticaria. Unfortunately, negative results were again obtained in experiments in which attempts were made to sensitize magnesium-deficient rats to uncooked egg white. After intraperitoneal injections of egg white and repeated multiple intradermal tests, no evidence of cutaneous or systemic hypersensitivity was forthcoming.

b. Therapy.—The response to therapy with magnesium sulfate is prompt in the case of experimental magnesium deficiency of the rat. By contrast, administration of magnesium sulfate to patients with disseminated neurodermatitis is of little or no value in the alleviation of the signs of the disease.

COMMENT

The important studies of Engman and MacCardle and MacCardle, Engman and Engman [7] have again focused attention on the significance of magnesium deficiency in relation to diseases

12. Kenton, H. B.: Arthus Phenomenon in Rat, J. Infect. Dis. **69**:238 (Nov.-Dec.) 1941.

of the skin. When these investigators stated that the experimental magnesium deficiency syndrome was the analogue of disseminated neurodermatitis it raised the hopes of dermatologists, for if their claim had proved to be true it would have provided the means for an experimental therapeutic approach to a chronic disease for which there is no uniformly satisfactory therapy. Unfortunately the contentions of MacCardle, Engman and Engman must be disclaimed when the signs and symptoms, the microscopic alterations and the chemical findings of the diseases are compared. In part I an attempt was made to compare the gross signs and the symptoms of the two diseases. The cutaneous lesion in the experimental animal differs in appearance and distribution. If there is any morphologic resemblance of the experimental disease to human dermatoses, urticaria and so-called toxic erythema would be more likely diseases with which to make comparisons. The occurrence of multiformed erythematous plaques and occasional bullae of the mucous membranes naturally suggests erythema multiforme as a disease that should be investigated in connection with magnesium deficiency. In the later stage of the disease, when there are scattered plaques of dermatitis on the trunk and snout, there occasionally may appear to be some resemblance of the experimental dermatosis to disseminated neurodermatitis. However, the distribution is not the same. In the experimental disease the flexor surfaces are rarely involved. Hyperpigmentation, which occurs in the human dermatosis, was not observed in the rat. The edema in the skin of the magnesium-deficient rat probably accounts for its increase in thickness. Pruritus, which is often distressing in man, is not a symptom of the disease in the rat. Excoriations are frequent in disseminated neurodermatitis, but ulcers of the peripheral parts, which occur in experimental magnesium deficiency, have never been observed in patients with disseminated neurodermatitis. Hepatitis has not been reported in connection with disseminated neurodermatitis. Nephritis, which almost invariably is an important feature of the experimental syndrome, occurs infrequently enough in patients with neurodermatitis to be considered an incidental complication. It is likely, however, that if statistics on this subject were assembled nephritis would be recorded as a complication of disseminated neurodermatitis in a higher percentage of cases than ordinarily would be predicted, especially in patients with extensive superimposed pyococcic infections. Convulsive seizures do not occur in patients with disseminated neurodermatitis. Hyperirritability is common to both diseases.

The microscopic changes are sufficiently diverse to dispel the notion of analogy. Although hyperemia is a finding common to both diseases it is more extensive in the experimental disease. The initial change in the experimental disease consists of edema in the lower part of the cutis and the subcutanea. There is no unformity of opinion [5b] concerning the exact site of initial cutaneous change in disseminated neurodermatitis; hence the important comparison regarding the primary site cannot be made. However, throughout the disease edema of the skin and subcutaneous tissues is a predominating sign in experimental magnesium deficiency. Also cellular infiltration is more pronounced in the experimental syndrome, and in some cases exudative cells encroach into the epidermis and result in focal areas of degeneration and necrosis. Hyperkeratosis is not always present and is usually not broad. In disseminated neurodermatitis the changes in the cutis do not include extensive edema. The epidermal changes in disseminated neurodermatitis differ from those of the experimental disease. Hyperkeratosis is a prominent feature of disseminated neurodermatitis. There is abundant intraepidermal edema, and there are peculiarities of staining which indicate that there has been a change in the chemical and physical constitution of the cells. According to MacCardle, Engman and Engman, the nuclei appear to be more fluid in consistency than normal cells and possess nucleoli that are composed of some abnormal substance probably akin to keratin. The spinous cells near the corneum are distended with some highly viscous coagulated products, such as a protein of homogeneous consistency.

The dissimilar chemical findings in the two diseases (part III) are sufficient to cast doubt on the proposition that the diseases are identical. The principal difference is that in the experimental disease there is a decrease of magnesium in the blood but not in the skin whereas in the human disease there is a decrease of absence of magnesium in the skin but no change in the blood level. Apparently in disseminated neurodermatitis the skin is unable to accept or retain biologically active magnesium, as the patients ingest and excrete magnesium in normal amounts.[5b, c] This is a fact that must be taken into account in considering disseminated neurodermatitis in relation to the experimental disease and also in appreciating the nature of disseminated neurodermatitis with no regard to its relation with the experimental disease.

The dissimilarity of disseminated neurodermatitis and experimental magnesium deficiency should not deter investigators from pursuing the answers to the questions concerning the relation of magnesium deficiency to disease. It is apparent from the study of the experimental disease in rats [1] and calves [2] that adequacy of magnesium in the diet is necessary for the maintenance of the integrity of the skin, the kidneys, the liver and the vascular system. It is apparent also that for some undetermined reason deficiency of magnesium may occur in the skin of man when the supply of magnesium in the diet is normal and the serum magnesium is not decreased. The question of the involvement of the parathyroids [5] has been suggested as an underlying or contributing factor in connection with magnesium deficiency, and research along these lines is desirable. Disconnected studies dealing with various aspects of magnesium deficiency indicate that it is an element which has received insufficient investigation, and it is likely that magnesium may prove to have a wider application in clinical medicine than it now enjoys. Soffer, Dantes, Grossman, Sobotka and Jacobs [13] reported a consistent increase in the nonultrafiltrable magnesium of the serum in patients with hyperthyroidism, whereas in 2 patients with myxedema all of the magnesium of the serum was ultrafiltrable. Dine and Lavietes [14] confirmed and extended the observations of Soffer and co-workers and found that in 14 normal subjects the nonultrafiltrable, or bound, fraction of the serum magnesium was 17 to 31 per cent of the total. In each of 9 patients with untreated proved hyperthyroidism, bound magnesium exceeded these values and the ultrafiltrable magnesium was subnormal. In 4 patients with myxedema, all of the magnesium of the serum was ultrafiltrable. After therapy for thyroid dysfunction the bound and ultrafiltrable magnesium returned to normal. On the basis of these findings Dine and Lavietes pointed out the possible relation of bound magnesium to the circulating thyroid hormone or to enzyme systems. As in the case of disseminated neurodermatitis, these investigators stated, the therapeutic applications of magnesium in treatment of thyroid disease were not yet determined. They were unable to duplicate the results of Hueber,[15] who claimed to have achieved regression of the symptoms of exophthalmic goiter and a reduction of the basal metabolism following injections of magnesium. Hirschfelder and Haury [16] showed that when normal persons ingested magnesium the concentration of the magnesium in the blood was not appreciably affected and that 40 per cent of the magnesium was excreted in the urine in twenty-four hours. They emphasized that under certain clinical conditions there were considerable variations in the concentration of magnesium in the plasma, and they described clinical syndromes of high and low concentrations of magnesium in the plasma. The former, hypermagnesemia, was accompanied by somnolence and coma and was induced in patients with renal insufficiency by the oral administration of one or more purgative doses of magnesium sulfate. The latter, hypomagnesemia, was accompanied by muscular twitching or by convulsions, and when it occurred in patients with renal insufficiency the twitchings or the convulsions were relieved by the oral administration of magnesium sulfate.

The mechanism whereby the signs of magnesium deficiency are produced has not been elucidated. The understanding of this interesting experimental syndrome was somewhat retarded by the contentions of Tufts and Greenberg [1c] who presented evidence purporting to show that complicating vitamin B complex deficiency was responsible for the signs attributed originally to magnesium deficiency by Orent and McCollum [1a] and Kruse, Orent and McCollum.[1b] Sullivan and Evans [1f] recently demonstrated that deficiencies of the vitamin B complex were not related to the signs produced by magnesium deficiency, and their findings removed one obstacle in the understanding of the syndrome. Whenever the subject of magnesium deficiency is presented, some discusser invariably expresses the objection that because of the widespread distribution of magnesium in natural foodstuffs, magnesium deficiency in man is probably rare, except possibly in patients with gastrointestinal disease. Granted that diets containing insufficient magnesium are not likely to be chosen by or forced on many human beings, it must be emphasized that inadequacy of an aliment in a diet and disease of the gastrointestinal tract preventing proper absorption are not the only means by which deficiency results. The concept

13. Soffer, L. J.; Dantes, D. A.; Grossman, E. B.; Sobotka, H., and Jacobs, M. D.: Ultrafiltrable Magnesium in Hyperthyroidism, J. Clin. Investigation **18**: 597 (Sept.) 1939.

14. Dine, R. F., and Lavietes, P. H.: Serum Magnesium in Thyroid Disease, J. Clin. Investigation **21**: 781 (Nov.) 1942.

15. Hueber, E. F.: Ueber die Beeinflussung von Hyperthyreosen durch Magnesiumglutaminat, Wien. klin. Wchnschr. **52**:932 (Oct. 13) 1939.

16. Hirschfelder, A. D., and Haury, V. G.: Clinical Manifestations of High and Low Plasma Magnesium, J. A. M. A. **102**:1138 (April 7) 1934.

of the avidin-biotin conditioning mechanism,[17] for example, has revised the narrow concept of excluding the probability of deficiency disease because of a history of an adequate diet. Other examples of conditioned deficiencies are now well known. The importance of the lack of antioxidants in experimental diets is presently the subject of interesting investigations regarding another mechanism for producing deficiency. It is becoming apparent also that disease of various organs or systems caused by metabolic disturbances and/or infections may result in disturbances affecting the normal utilization of a particular aliment that may be abundantly ingested. In disseminated neurodermatitis there is a deficiency of magnesium in the skin although not in the diet and in the serum. This suggests that intensive investigation should be directed toward the clarification of the interrelationship of calcium, phosphorus and magnesium metabolism, as magnesium deficiency in the skin may be the indirect result of a disease of organs which control or participate in calcium and phosphorus metabolism. The investigations of Engman and MacCardle and of MacCardle, Engman and Engman[5] were undertaken because little was known about the mineral content of the skin in health and in disease and electrolytes are known to play a part in the phenomena of osmosis and surface tension. These investigators expressed the opinion that electrolytes and other powerful interacting physical forces probably enter into the production of various phases of inflammation and the permeability of the capillaries of the skin and of the epithelial cell membranes may be influenced greatly by the quality and quantity of the minerals in the cell and in its environment.

Although it was not possible to establish the claim[5] that disseminated neurodermatitis and experimental magnesium deficiency were identical or similar diseases, we wish to emphasize the importance of the studies of Engman and MacCardle, and MacCardle, Engman and Engman, and to encourage dermatologists to interest themselves in the complexities and possibilities of magnesium deficiency in relation to disease.

17. (*a*) Eakin, R. A.; Snell, E. E., and Williams, R. J.: A Constituent of Egg White Capable of Inactivating Biotin in Vitro, J. Biol. Chem. **136**:801 (Dec.) 1940. (*b*) György, P.; Rose, C. S.; Eakin, R. E.; Snell, E. E., and Williams, R. J.: Egg White Injury as the Result of Non-Absorption or Inactivation of Biotin, Science **93**:477 (May 16) 1941. (*c*) Sullivan, M., and Nicholls, J.: Nutritional Dermatoses in the Rat: V. Signs and Symptoms Resulting from a Diet Containing Unheated Dried Egg White as the Source of Protein, Arch. Dermat. & Syph. **45**:295 (Feb.) 1942.

SUMMARY AND CONCLUSIONS

When disseminated neurodermatitis and experimental magnesium deficiency in rats were compared, it was found that they are not similar diseases.

The relation of magnesium deficiency to disease merits further study.

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THE ALOE VERA PLANT

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A number of interesting articles have appeared giving quaint historical lore and scientific application of the Aloe vera leaf for dermatologic purposes.[1] Particular application of the leaf has been recommended in radiodermatitis. The first article published on the use of the Aloe vera leaf in radiodermatitis was written by C. E. Collins and Creston Collins.[1b] Dr. C. E. Collins[2] first

Fig. 1.—Close-up view of the Aloe vera plant.

became interested in the therapeutic use of the leaves in 1935, his son Dr. Creston Collins having seen the Seminole Indians using the leaf of the plant to treat burns. These physicians then applied the leaf for the treatment of radiodermatitis, with encouraging results. Since then, it has become widely used for this purpose.

In New York the leaf is a relatively rare and expensive product, often kept wrapped in tinfoil and usually refrigerated. (It is best kept at room temperature.) Recently while in Miami I was able to observe several thousands of these plants being grown for commercial purposes. I was fortunate in being able to visit an Aloe vera farm, which is located about 25 miles (40 kilometers) southwest of Miami. This farm is one of several in the vicinity.

There are several varieties of Aloe, one of which, Aloe perryi (Baker), or socotrine aloe, seems to have been produced in the island of Socotra at least as early as the time of Alexander the Great, 333 B.C. The main reason for its cultivation is to obtain aloe, the dried juice of the leaves of the various species of Aloe.

The Dispensatory of the United States of America mentions that aloe was known to the ancients and used as a cathartic and a vulnerary. No mention is made of any dermatologic value. The various species differ considerably in size and in appearance. To describe the botanic aspects, I can best quote from the Dispensatory[3]:

> The true Socotrine aloe has a trunk one foot high which bears upon its summit a dense rosette of pale green or reddish succulent, lanceolate leaves. The Aloe Vera has a very short, woody stem, and lanceolate embracing leaves, which are first spreading, then ascending, of a glaucous green color, when young, irregularly mottled with white spots, flat on the upper surface, convex beneath, and armed with hard pale spines, flat on the upper surface distant from each other, and perpendicular to the margin. It has bright yellow flowers arranged in a spicate inflorescence.

The entire plant is about 2 feet (60 cm.) high. The flowers are almost a foot higher when they are in bloom. It takes about five years for the plants to bear leaves which are used commercially. One or more leaves can then be cut about every two months. Usually leaves weighing about 1 pound (4.5 Kg.) are selected for dermatologic use. Locally in Florida the plant has a provincial reputation for curing many ailments,

Fig. 2.—Split leaf showing mucilaginous liquid exuding from the cut surfaces, and also the relative size of the leaf.

particularly of the skin. In addition, it has the virtue of "cleansing the innards" when drunk as a brew. This of course is due to the high aloe content of the leaf.

1. (*a*) Cole, H. N., and Chen, K. K.: Aloe Vera in Oriental Dermatology, Arch. Dermat. & Syph. **47**:250 (Feb.) 1943. (*b*) Collins, C. E., and Collins, C.: Roentgen Dermatitis Treated with Fresh Whole Leaf of Aloe Vera, Am. J. Roentgenol. **33**:396 (March) 1935. (*c*) Tchou, M. T.: Aloe Vera (Jelly Leeks), Arch. Dermat. & Syph. **47**:249 (Feb.) 1943.

2. Collins, C. E.: Personal communication to the author.

3. Wood, H. C., and others: The Dispensatory of the United States of America, ed. 22, Philadelphia, J. B. Lippincott Company, 1937.

SEVERE ERYTHEMA MULTIFORME

REPORT OF TWO CASES OF THE TYPE ECTODERMOSIS EROSIVA PLURIORIFICIALIS, WITH DEVELOPMENT OF CICATRICIAL CONJUNCTIVITIS AND KERATITIS IN ONE CASE

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In most cases erythema multiforme runs a mild course free from alarming symptoms. Nevertheless, cases of severe forms of this disease have occasionally been reported. Severe erythema multiforme differs from the common form in the following ways: High fever and severe constitutional symptoms are present; the cutaneous eruption is more extensive, with vesicular and bullous lesions predominating, and there is severe involvement of the mucous membranes.

Erythema multiforme with severe and predominant involvement of the mucous membranes has in the past often not been recognized as erythema multiforme and therefore cases have been reported under names such as *"ectodermose érosive pluriorificielle"* (Rendu [1] and Fiessinger [2]), "dermatostomatitis" (Baader [3]) and "eruptive fever with stomatitis and ophthalmia" (Stevens and Johnson [4]).

In this communication the course and manifestations of severe erythema multiforme will be discussed and 2 cases which were recently observed at the Massachusetts General Hospital will be reported.

COURSE OF SEVERE ERYTHEMA MULTIFORME

Severe erythema multiforme starts abruptly with severe malaise and fever. The patient soon becomes prostrated and often delirious. The temperature may reach 104, 105 or even 106 F. Simultaneously or within a few days, an eruption appears on the skin, which at first is usually composed of macules and papules but soon becomes predominantly vesicular and bullous. The mucous membranes are almost always affected. Their involvement is usually severe and may dominate the clinical picture. The oral, pharyngeal, laryngeal, tracheal, bronchial, nasal and anal mucous membranes as well as the conjunctivas and the glans penis may be involved. The mucous membranes may show lesions before any have appeared on the skin. Frequently the first manifestations are found on the oral mucosa. Occasionally the first lesions develop in the pharynx or the upper respiratory tract, in which case the onset is like that of an infection of the upper respiratory tract. In the course of the disease extensive painful erosions may develop in the oropharynx at the sites of broken bullae. Concomitant edema of the larynx and trachea may cause severe dyspnea, and the tracheal and bronchial lesions may lead to the development of bronchopneumonia; hence the patient appears to be in an alarming condition. The stage of acute emergency lasts, however, only a few days, after which time the number of new lesions quickly diminishes. Cutaneous lesions usually cease to form after a period of from one to four weeks, and no scarring remains. In some cases, lesions on the mucous membranes, though usually few, continue to form for several months before healing, also without scarring, takes place. In contrast to all other lesions, those of the conjunctiva can be destructive and can persist for many years. In some cases a purulent conjunctivitis during the acute stage leads to maceration and perforation of the cornea and causes a panophthalmitis resulting in blindness. In other cases the conjunctivitis persists for many years and gradually leads to shrinking of the conjunctiva and to corneal ulcerations, resulting in considerable impairment of the patient's vision.

Even in the cases with the most acute and alarming symptoms at the onset, the disease rarely ends in death. Only 4 fatal cases of erythema multiforme were found in the literature. Regarding the well known tendency of the disease to occur, it appears from the literature that severe erythema multiforme is rarely preceded by any attacks and that subsequent attacks are usually milder.

From the Dermatologic Department of the Massachusetts General Hospital, C. Guy Lane, Chief.

1. Rendu, R.: Sur un syndrome caractérisé par l'inflammation simultanée de toutes les muqueuses externes (conjunctivale, nasale, linguale, bucco-pharyngée, anale et balano-préputiale) coexistant avec une éruption varicelliforme puis purpurique des quatre membres, Rev. gén. de clin. et de thérap. **30**:351, 1916.

2. Fiessinger, N., and Rendu, R.: Sur un syndrome caractérisé par l'inflammation simultanée de toutes les muqueuses externes coexistant avec une éruption vésiculeuse des quatre membres, non douloureuse et non récidivante, Paris méd. **25**:54, 1917.

3. Baader, E.: Dermostomatitis, Arch. f. Dermat. u. Syph. **149**:261, 1925.

4. Stevens, A. M., and Johnson, F. C.: A New Eruptive Fever Associated with Stomatitis and Ophthalmia, Am. J. Dis. Child. **24**:526 (Dec.) 1922.

MANIFESTATIONS OF SEVERE ERYTHEMA MULTIFORME

1. Cutaneous Lesions.—The lesions of erythema multiforme may be predominantly cutaneous or predominantly mucosal. Only in rare instances are cutaneous lesions completely absent, as, for instance, in the cases reported by Rissom,[5] Jordan,[6] Hoffmann,[7] Butler,[8] Fiessinger, Wolff and Thévenard[9] and Mach, Babel and Neville.[10] The cutaneous eruption has a predilection for the extremities. In severe forms, however, this may hold true only at the onset, while at the height of the disease the eruption may show a generalized distribution. At the onset the cutaneous eruption is composed of macules and papules with a tendency to confluence. In severe erythema multiforme the erythematous lesions soon become bullous, and at the height of the disease newly erupting lesions are bullous from their first appearance. The bullae may develop on an erythematous base or on normal-appearing skin. They usually are flaccid, break easily and leave erosions. The erosions tend to enlarge as the epithelium becomes detached at the periphery. By peripheral extension and confluence of the erosions large denuded areas may develop. The clinical picture at the height of the disease closely resembles that of pemphigus vulgaris. The course of the two diseases, however, is different, as will be discussed later.

2. Lesions of the Mucous Membranes.—(*a*) Lesions of the Oral and Laryngeal Mucosa: Oral lesions usually are bullous from the onset. The bullae break soon after formation, and extensive erosions result. The lips, gums and tongue may show considerable swelling. There is increased salivation, and the sputum is tinged with blood. Hemorrhagic crusts form over the erosions on the lips. In the severest stage almost the whole oral mucosa may be transformed into one large eroded surface. The lesions may extend into the pharynx and larynx. The accompanying laryngeal edema may cause severe dyspnea. That such severe involvement of the oral and laryngeal mucosa may occur in erythema multiforme has not been generally known until relatively recent years. For this reason, Rendu[1] in 1916 and shortly thereafter Fiessinger and Rendu[11] believed that they were dealing with a disease not previously described, when they observed a series of cases presenting a severe bullous erosive stomatitis associated with similar lesions of the conjunctival, nasal, anal and penile mucous membranes and a "varicelliform" cutaneous eruption located mainly on the extremities. Fiessinger[9] chose the name *ectodermose érosive pluriorificielle.* Rendu and Fiessinger noted the resemblance to erythema multiforme but believed that it was not the same disease because of the predominance of mucosal lesions, the severe febrile course and the absence of recurrences in any of their cases. Following Rendu's and Fiessinger's reports several French writers published reports of similar cases under the designation *ectodermose érosive pluriorificielle,* still believing that they were dealing with a new, probably infectious, disease. Among them were Grysez and Pierret,[12] Fiessinger, Wolff and Thévenard,[9] de Lavergne[13] and Schreuder.[14] Subsequent reporters of cases of this syndrome, like Jansion and Diot[15] and Janbon, Ratié and Bétoulières[16] in France, Kumer[17] in Germany, Fanconi[18] and Mach, Babel and Neville[10] in Switzerland and Klauder[19] in the United States, firmly established the identity of ectodermosis

5. Rissom: Erythema bullosum der Mundschleimhaut, Dermat. Ztschr. **15**:583, 1908.

6. Jordan, A.: Bemerkungen zur Frage des Erythema exsudativum multiforme, Dermat. Ztschr. **29**:89, 1920.

7. Hoffmann, E., in discussion on Jordan.[6]

8. Butler, J.: Erythema Multiforme Confined to the Mucous Membranes, Arch. Dermat. & Syph. **6**:1 (July) 1922.

9. Fiessinger, N.; Wolff, M., and Thévenard, A.: Ectodermose érosive pluri-orificielle, Bull. et mém. Soc. méd. d. hôp. de Paris **47**:446, 1923.

10. Mach, R. S.; Babel, J., and Neville, M.: Syndromes muco-cutanés avec complications oculaires (erythème polymorphe, iritis récidivante aphtheuse), Helvet. med. acta **7**:552, 1941.

11. Rendu, R.: Six nouveau cas d'une maladie infectieuse caractérisée par l'inflammation des muqueuses conjunctivale, nasale, bucco-pharyngée et préputiale, et, accessoirement par une éruption vésico-bulleuse des membres, Presse méd. **25**:662, 1917. Fiessinger and Rendu.[2]

12. Grysez and Pierret: Spirillose généralisée, Presse méd. **25**:662, 1917.

13. de Lavergne: A propos de la communication de MM. Fiessinger, Wolff et Thévenard sur l'ectodermose érosive pluri-orificielle, Bull. et mém. Soc. méd. d. hôp. de Paris **47**:462, 1923.

14. Schreuder, J. J. C.: Een beval von ectodermosis erosiva pluri-orificialis bij eene vrouw, Nederl. tijdschr. v. geneesk. **1**:874, 1926.

15. Jansion, H., and Diot: Sur les rapports de l'ectodermose érosive pluri-orificielle de Fiessinger, Wolff et Thévenard avèc l'hydroa vésiculeux de Bazin, Ann. de dermat. et syph. **6**:440, 1925.

16. Janbon, M.; Ratié, A., and Bétoulières, P.: Deux observations d'ectodermose bulleuse, Arch. Soc. d. sc. méd. et biol. de Montpellier **15**:573, 1934.

17. Kumer, L.: Ectodermose érosive pluriorificielle und Erythema exsudativum multiforme, Dermat. Ztschr. **72**:62, 1935.

18. Fanconi: Ectodermose érosive pluriorificielle: Leichte meningitische Reizung, Bienenhonigidiosynkrasie, Schweiz. med. Wchnschr. **72**:475, 1942.

19. Klauder, J. V.: Ectodermosis Erosiva Pluriorificialis: Its Resemblance to the Human Form of Foot and Mouth Disease and Its Relation to Erythema Exsudativum Multiforme, Arch. Dermat. & Syph. **36**: 1067 (Nov.) 1937.

erosiva pluriorificialis with erythema multiforme. It is believed, in accordance with the opinions of these authors, that ectodermosis erosiva pluriorificialis represents erythema multiforme with severe involvement of the oral and other mucous membranes and that this term may be used as designation for such conditions. Baader [3] in 1925 selected still another name, "dermatostomatitis," as the diagnostic term in 4 cases of severe erythema multiforme with predominantly oral lesions. Only two other authors, namely Moncorps [20] and Storck,[21] have reported cases under this name. The identity of dermatostomatitis and erythema multiforme has been pointed out by Klauder [19] and by Low and Davies.[22]

(*b*) Conjunctival Lesions: Conjunctival lesions are not uncommon in erythema multiforme. Von Düring [23] in a series of 105 cases observed conjunctivitis in more than three quarters of the cases. Duke-Elder [24] distinguished three forms of conjunctivitis in erythema multiforme, namely a catarrhal form, a purulent form and a pseudomembranous form. He regarded them, however, as different only in degree of severity. Transitions between the three forms and their combinations may be observed. The mildest and most common form of conjunctival erythema multiforme is the catarrhal form. This form tends to heal within a few weeks and does not cause permanent damage to the eyes. The second form of conjunctivitis, the purulent form, if suppuration is profuse may lead to maceration and ulceration of the cornea, with subsequent corneal perforation and panophthalmitis. Such severe destruction of the eyes is fortunately extremely rare. Only 4 cases were found in the literature. The first 2 cases were reported by Stevens and Johnson [4] under the title "A New Eruptive Fever Associated with Stomatitis and Ophthalmia." The other 2 cases were reported by Wheeler [25] and Ginandes.[26] In the third form, the pseudomembranous, the tarsal conjunctivas appear infiltrated and possess a rubbery, brownish red appearance. Pseudomembranes form on the tarsal conjunctivas, and there is a mucoid, stringy discharge. Considerable photophobia exists but little actual pain. In milder forms the lesions may heal in a few weeks without scarring. When the disease is more severe, however, the conjunctival lesions persist for years. In the course of months scarring of the conjunctivas, with obliteration of the fornices and formation of adhesions between the bulbar and the palpebral conjunctiva, develops, and superficial corneal ulcerations may leave corneal opacities. In the chronic stage the clinical picture is identical with that of pemphigus conjunctivae and that observed in the so-called third stage of trachoma. Cases of pseudomembranous conjunctivitis without subsequent scarring have been reported, for instance, by Fuchs,[27] Gerke and Kain,[28] Hartlev [29] (case 2), Koke [30] (case 1) and Storck [21] (case 1). Cases with conjunctival and corneal scarring have been reported by Hanke,[31] Barkan,[32] Stark,[33] Hartlev [29] (case 1), Raffin,[34] Rutherford [35] and Bailey.[36] Cases which were reported as instances of pemphigus conjunctivae but which because of the sudden, acute onset and the short duration of the accompanying cutaneous and oral lesions are considered to have been cases of erythema multiforme include those of Albrand,[37] Glas [38] and Mayou.[39]

20. Moncorps, C.: "Dermatostomatitis"—eine Grippekomplikation, Arch. f. Dermat. u. Syph. **150**:104, 1926.

21. Storck, H.: Dermatostomatitis (Baader) oder Ectodermose érosive pluriorificielle im Kindesalter, Schweiz. med. Wchnschr. **72**:1102, 1942.

22. Low, E. B., and Davies, J. H. T.: Dermato-Stomatitis (Baader), Complicating a Case of Manic-Depressive Insanity, Brit. J. Dermat. **50**:141, 1938.

23. von Düring, E.: Beitrag zur Lehre von den polymorphen Erythemen, Arch. f. Dermat. u. Syph. **35**:211, 1896.

24. Duke-Elder, W. S.: Erythema Exudativum Multiforme (Hebra), in Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2, p. 1733.

25. Wheeler, J. M.: Destructive Purulent Ophthalmia Accompanying an Eruptive Fever with Stomatitis, Tr. Am. Acad. Ophth. **34**:179, 1929.

26. Ginandes, G. J.: Eruptive Fever with Stomatitis and Ophthalmia, Am. J. Dis. Child. **49**:1148 (May) 1935.

27. Fuchs, E.: Herpes Iris Conjunctivae, Klin. Monatsbl. f. Augenh. **14**:333, 1876.

28. Gerke, O., and Kain, E.: Ein Fall von Croup der Bindehaut, der Mund- und Rachenschleimhaut, Arch. f. Augenh. **24**:305, 1892.

29. Hartlev, C. C.: Ueber die Kombination der Conjunctivitis et stomatitis pseudomembranacea und ihr Verhältnis zum Erythema multiforme und Pemphigus, Klin. Monatsbl. f. Augenh. **67**:223, 1921.

30. Koke, M. P.: Conjunctivitis in Erythema Exudativum Multiforme, Arch. Ophth. **25**:78 (Jan.) 1941.

31. Hanke, V.: Der Herpes iris des Auges, Arch. f. Ophth. **52**:263, 1901.

32. Barkan, H.: Herpes Iris of the Conjunctiva, with Report of a Case, Arch. Ophth. **42**:236, 1913.

33. Stark, H. H.: Membranous Conjunctivitis of Four Years' Duration, Am. J. Ophth. **1**:91, 1918.

34. Raffin, A.: Conjunctivitis, Rhinitis und Stomatitis aphthosa mit Erythema multiforme, Klin. Monatsbl. f. Augenh. **68**:216, 1922.

35. Rutherford, C. W.: Membranous Conjunctivitis with Loss of the Eyeballs, J. A. M. A. **93**:1779 (Dec. 7) 1929.

36. Bailey, J. H.: Lesions of the Cornea and Conjunctiva in Erythema Exudativum Multiforme (Hebra), Arch. Ophth. **6**:362 (Sept.) 1931.

37. Albrand, W.: Ueber Pemphigus conjunctivae, Klin. Monatsbl. f. Augenh. **32**:220, 1894.

38. Glas: Pemphigus conjunctivae, Klin. Monatsbl. f. Augenh. **33**:17, 1895.

39. Mayou, M. S.: ? Acute Pemphigus of the Conjunctiva, Proc. Roy. Soc. Med. (Sect. Ophth.) **20**:427, 1926-1927.

(*c*) Lesions of the Anal Mucosa and Glans Penis: Lesions of the anal mucosa and glans penis are not infrequently observed. I have failed, however, to find reports of any case in which the anal lesions caused a prolapse of the anal mucosa and subsequent sloughing, as in the first of the 2 cases in the present report. Adhesions between the prepuce and the glans penis, as observed in case 2, have been reported in only 1 other case, by Klauder [19] (case 2).

(*d*) Tracheal, Bronchial and Bronchiolar Lesions: Involvement of the tracheal, bronchial and bronchiolar mucous membranes, although not mentioned in any of the current textbooks, appears well established from the number of cases reported. Tracheobronchial involvement may be one of the first symptoms or may develop in the course of the disease. It causes production of large amounts of mucopurulent sputum which the patient raises with difficulty. Accumulation of the sputum in the trachea may lead to attacks of dyspnea. In cases of severe tracheobronchitis bronchopneumonia may develop. The occurrence of tracheobronchitis with erythema multiforme has been reported, for instance, by Hanke [31] (case 2), Blair,[40] Welander,[41] Salus [42] (case 1), Hartley [20] (case 1), Stevens and Johnson,[4] Raffin,[34] de Lavergne [13] (case 1), Baader [3] (cases 1 and 2), Smith,[43] Bailey [36] (cases 1 and 2), Janbon, Ratié and Bétoulières [16] (case 2), Klauder [19] (case 2), Low and Davies [22] and Storck.[21] In the cases reported by Hanke,[31] Welander [41] and Smith [43] bronchopneumonia as a complication of the tracheobronchitis caused the death of the patient.

3. Articular Lesions.—Pains in joints occasionally occur early in the disease. They usually last only a few days. There may or may not be any swelling of the affected joints.

4. Intestinal Lesions.—It is rather dubious whether or not intestinal lesions occur in patients with erythema multiforme. Only 2 cases with intestinal lesions were found reported in the literature. Neither report is convincing. Hebra,[44] who did not mention any other mucosal lesions in erythema multiforme, reported briefly the case of a woman who had "erythema gyratum and died from it" and in whom the autopsy revealed "in the small bowels similar red circles as on the skin." Hanke [31] reported a case of erythema multiforme with severe stomatitis which spread to the pharynx "and apparently also to the lungs and stomach because of sudden pulmonary edema and hematemesis." In the autopsy report pulmonary but no intestinal lesions are mentioned. Intestinal lesions in erythema multiforme have also been reported by Osler [45] and de Amicis,[46] but, as will be discussed later, a diagnosis of erythema multiforme does not seem justified in these cases.

5. Renal Lesions.—No renal involvement seems to occur in erythema multiforme, with the exception of transient albuminuria, which has been reported in cases of the severe form. In cases reported as instances of erythema multiforme with renal involvement either the disease was not erythema multiforme, as in Osler's cases, or the erythema multiforme developed in addition to a previously existing renal disease, as in the cases reported by Sachs [47] and Ledermann.[48]

MORTALITY

In spite of the severe initial symptoms, death from erythema multiforme is rare. Only 4 cases of death are on record. It is, however, likely that some fatal cases reported as cases of pemphigus acutus were in reality instances of erythema multiforme. The relation between pemphigus acutus and erythema multiforme will be discussed in conjunction with the differential diagnosis. In 3 of the fatal cases, namely those reported by Hanke,[31] Welander [41] and Smith,[43] death was due to bronchopneumonia. In the fourth fatal case, reported by Corlett,[49] no oral or bronchial lesions were present. The

40. Blair, L. E.: A Case of Recurring Membranous Stomatitis, Associated with Erythema Exudativum Multiforme (Hebra), M. Rec. **65**:729, 1904.

41. Welander, E.: Ein Fall von Erythema multiforme exsudativum mit tötlichem Ausgang, Arch. f. Dermat. u. Syph. **77**:289, 1905.

42. Salus, R.: Erythema exsudativum multiforme am Auge, Klin. Monatsbl. f. Augenh. **50**:30, 1912.

43. Smith, C. A.: Unusual Case of Erythema Multiforme, Tr. Univ. Michigan Pediat. & Infect. Dis. Soc., 1929, p. 63.

44. Hebra, F., and Kaposi, M.: Erythema exsudativum multiforme, in Lehrbuch der Hautkrankheiten, ed. 2, Erlangen, F. Enke, 1874, vol. 1, p. 249.

45. Osler, W.: (*a*) On the Visceral Complications of Erythema Exudativum Multiforme, Am. J. M. Sc. **110**:629, 1895; (*b*) The Visceral Lesions of the Erythema Group, Brit. J. Dermat. **12**:227, 1900; (*c*) On the Visceral Manifestations of the Erythema Group of Skin Diseases, Am. J. M. Sc. **127**:1, 1904.

46. de Amicis, A.: Ein Fall von Erythema exsudativum multiforme haemorrhagicum mit Exitus letalis, Arch. f. Dermat. u. Syph. **116**:461, 1913.

47. Sachs, O.: Beziehungen zwischen dem Erythema exsudativum multiforme und den Erkrankungen innerer Organe, Arch. f. Dermat. u. Syph. **98**:35, 1909.

48. Ledermann, R.: Ueber Erythema multiforme als Symptom einer schweren Allgemeinerkrankung, Med. Klin. **4**:698, 1908.

49. Corlett, W. T.: Erythema Exudativum Multiforme: Its Present Significance with a Report of a Case of Erythema Circinatum Bullosum et Haemorrhagicum Following a Gunshot Wound, Apparently Due to Streptococcus Infection and Terminating Fatally, J. Cutan. Dis. **26**:7, 1908.

cutaneous lesions were extensive, and there were large denuded areas.

Fatal cases of a disease diagnosed as erythema multiforme have also been reported by Osler and de Amicis. In three communications [45] Osler reported a total of 29 cases, with 7 deaths. Osler stressed the frequency of visceral lesions in erythema multiforme and the serious course which the disease may take when they are present. Duhring [50] objected to the diagnosis of erythema multiforme at the time of publication of Osler's first paper and regarded most of the 7 cases of Osler's first communication as cases of purpura. In a fourth paper,[51] published in 1914, ten years later than the third paper, Osler himself referred to his series of 29 cases as cases of Henoch's purpura. In modern classification the majority of Osler's 29 cases would be regarded as instances of either Henoch's or Schönlein's purpura. Some (cases 12, 17 and 25) were cases of urticaria with abdominal colics; 2 (cases 19 and 26) were cases of acute lupus erythematosus. Only 1 patient (case 13) had erythema multiforme. In this case the eruption lasted sixteen days and the disease was not fatal. Attacks of colic which occurred showed no obvious relation to the erythema multiforme, since they preceded the eruption by six months and continued after the eruption had healed. De Amicis' [46] case also appears to have been a case of Henoch's purpura. The cutaneous lesions were macular, papular and purpuric. At autopsy almost the entire intestinal tract was found to be hemorrhagic. The lungs and spleen showed hemorrhagic infarcts, and there were petechiae on the pericardium.

DIFFERENTIAL DIAGNOSIS

Three diseases have to be considered in the differential diagnosis of severe erythema multiforme: eruption due to a drug, foot and mouth disease and pemphigus vulgaris.

1. Eruption Due to Drug.—Bullous eruptions of the skin and mucous membranes resembling erythema multiforme may be produced by several drugs. The resemblance is often so great that many authors distinguish between idiopathic and symptomatic erythema multiforme. The most common drugs to cause bullous eruptions are inorganic arsenic, iodine, phenolphthalein, antipyrine, the barbiturates and the sulfonamide compounds.

Bullous eruptions due to inorganic arsenic are rare. They usually are not extensive and do not involve the mucous membranes. Bullous eruptions caused by iodine are nearly always limited to exposed areas, namely the face, neck and hands, and there is a tendency to formation of vegetations at the site of lesions. Phenolphthalein and antipyrine may produce erythema-multiforme-like eruptions of the skin and mucous membranes. Although large bullous lesions have been described as occurring in eruptions due to phenolphthalein, none of the patients in the reported cases had lesions of the extent and severity of those in the 2 cases of ectodermosis erosiva pluriorificialis reported in this paper. Barbiturates cause morbilliform and scarlatiniform eruptions most frequently. In severe forms the eruption may progress to the development of vesicles and bullae. Involvement of the mucous membranes is common in patients with severe eruptions. Moss and Long [52] reported 2 cases of severe bullous lesions of the skin and mucous membranes following the use of phenobarbital and pointed out the close resemblance to ectodermosis erosiva pluriorificialis. They expressed the belief that in some cases reported under this diagnosis phenobarbital may have been the causative factor. Cutaneous eruptions caused by the sulfonamide compounds are also most frequently morbilliform and scarlatiniform, but occasionally they are bullous. Oral lesions are rare. Raffetto and Nichols [53] and Greenberg and Messer [54] have reported 2 cases in which a severe bullous eruption of the skin and mucous membranes developed after use of sulfadiazine. The clinical picture in both cases resembled ectodermosis erosiva pluriorificialis in every respect. In these 2 cases sulfadiazine was given because of the presence of an infection of the upper respiratory tract. Whether sulfadiazine actually produced the eruption or whether the so-called infection of the upper respiratory tract was the first symptom of an idiopathic ectodermosis erosiva pluriorificialis is impossible to decide.

2. Foot and Mouth Disease.—The oral and other mucosal lesions of foot and mouth disease may closely resemble those of erythema multiforme. The cutaneous lesions usually are limited to the skin near the mucocutaneous junctions and to the fingers and toes. Klauder [19] and Raffin [34] expressed the belief that in some of

50. Duhring, L. A., cited by Osler.[45b]

51. Osler, W.: The Visceral Lesions of Purpura and Allied Conditions, Brit. M. J. **1**:517, 1914.

52. Moss, R. E., and Long, W. E.: Toxic Eruptions Due to Phenobarbital, Arch. Dermat. & Syph. **46**:386 (Sept.) 1942.

53. Raffetto, J. F., and Nichols, S.: A Nearly Fatal Reaction to Sulfadiazine in a Ten-Year Old Girl Involving Skin, Eyes and Oropharynx, J. Pediat. **20**: 753, 1942.

54. Greenberg, S. I., and Messer, A. L.: Fatal Bullous Dermatitis Following Administration of Sulfadiazine, J. A. M. A. **122**:944 (July 31) 1943.

the cases reported as instances of the human form of foot and mouth disease in which laboratory animals were not inoculated the disease was erythema multiforme. Raffin mentioned as examples the cases reported by Schultz [55] and Illig.[56] In the latter case a recurrence of the eruption eight weeks after the first eruption had subsided makes a diagnosis of erythema multiforme likely.

3. Pemphigus Vulgaris.—Distinction of severe erythema multiforme from pemphigus vulgaris may be extremely difficult at the height of the disease. The onset and the course of the two diseases are, however, entirely different. Even in the cases of pemphigus vulgaris in which the disease takes an acute course the onset is less abrupt. The bullous eruption extends gradually, and high fever, if it appears at all, develops only in the course of the disease. Sudden dramatic improvement is most uncommon, and tracheobronchial involvement, with expectoration of large amounts of mucopurulent sputum, does not occur. Furthermore, pemphigus vulgaris is most common in middle age and old age, while erythema multiforme is predominantly a disease of children and young adults.

A considerable number of cases of acute bullous eruptions have been reported under the designation of pemphigus acutus, or "butcher's pemphigus." It will be shown in a future communication that most if not all of the conditions described under this term can be given a different diagnosis and that therefore the diagnostic term pemphigus acutus, or "butcher's pemphigus," can be discarded. If those diseases which obviously were bullous impetigo are eliminated, most cases reported as pemphigus acutus can be classified either as cases of pemphigus vulgaris with an acute course or as cases of erythema multiforme. Among those cases which can be regarded as cases of erythema multiforme there are many of the type of ectodermosis erosiva pluriorificialis. As examples one might mention the cases reported by Burrows [57] (case 1), Horand [58] (case 2), Southey,[59] Senftleben,[60] Senator,[61] Marijo,[62] Fabre,[63] Dolega,[64] Jónsson,[65] Richardière,[66] Penny,[67] Saundby,[68] Winfield,[69] Arning,[70] Custance,[71] Luithlen [72] (case 1), Berling,[73] Roederer and Lanzenberg,[74] Stokes [75] and Kinnear [76] (case 2). All these reports concern patients who were severely ill at the onset of the disease and had extensive cutaneous and mucosal lesions but who recovered within a few weeks. In 3 of these cases, namely those reported by Richardière, Penny and Winfield, the patient had more than one attack of the disease. It is likely that even some of the cases reported as instances of fatal pemphigus acutus were actually cases of severe erythema multiforme of the type ectodermosis erosiva pluriorificialis. This possibility is considered in the fatal cases reported by Horand [58] (case 1), Purjesz,[77] Spillmann,[78] Danek,[79] Robinson,[80] Cleveland [81] and Kinnear [76] (case 1).

55. Schultz, W.: Zur Differentialdiagnose der Maul- und Klauenseucheninfektion beim Menschen, Med. Klin. **15**:817, 1919.

56. Illig, H.: Aphthae epizooticae beim Menschen mit besonderer Berücksichtigung der Augensymptome, Arch. f. Augenh. **83**:64, 1917-1918.

57. Burrows, G.: A Vesicular Disease Contracted from Sheep, M. Times & Gaz. **1**:589, 1856.

58. Horand: Note pour servir à l'histoire du pemphigus aigu fébrile, Ann. de dermat. et syph. **4**:401, 1872-1873.

59. Southey, R.: Acute Pemphigus, Tr. Clin. Soc. London **8**:179, 1875.

60. Senftleben: Ein Fall von Pemphigus acutus, Berl. klin. Wchnschr. **17**:456, 1880.

61. Senator, H.: Ein Fall von Pemphigus acutus (Febris bullosa), Deutsche med. Wchnschr. **12**:3, 1886.

62. Marijo, J. A.: Un cas de pemphigus aigu, Gaz. hebd. d. sc. méd. de Montpellier **10**:613, 1888.

63. Fabre, P.: Pemphigus aigu généralisé, Gaz. méd. de Paris **6**:509, 1889.

64. Dolega: Ein Fall von Pemphigus acutus mit acuter hämorrhagischer Nephritis beim Erwachsenen, Deutsches Arch. f. klin. Med. **45**:101, 1889.

65. Jónsson, J.: Acute Pemphigus, Lancet **1**:736, 1897.

66. Richardière, H.: Note sur deux cas de pemphigus aigu, Bull. méd., Paris **11**:189, 1897.

67. Penny, E.: A Case of Acute Herpetic Pemphigus, Arch. Surg., London **10**:239, 1899.

68. Saundby, R.: Acute Pemphigus in a Butcher's Boy Resulting in Recovery, Lancet **2**:946, 1904.

69. Winfield, J. McF.: Pemphigus and Bullous Dermatoses, and Notes on Some Personally Observed Cases, J. Cutan. Dis. **26**:566, 1908.

70. Arning: Fall von Pemphigus malignus acutus, Arch. f. Dermat. u. Syph. **112**:417, 1912.

71. Custance, G. W. M.: Acute Pemphigus Due to Infection by a Diplococcus: Treatment by Autogenous Vaccine; Diagnosis Complicated by the Presence of a Positive Wassermann, Practitioner **91**:710, 1913.

72. Luithlen, F.: Pemphigus acutus (Blasenausschlag bei Sepsis und Dysenterie); Heilung durch Aderlass und Eigenserum, Wien. klin. Wchnschr. **31**:1297, 1918.

73. Berling, W.: Ein kasuistischer Beitrag zur Lehre von Pemphigus acutus oder Febris bullosa, Inaug. Dissert., Greifswald, H. Adler, 1918.

74. Roederer, M. J., and Lanzenberg, P.: Dermatose bulleuse fébrile allant vers le pemphigus aigu, mais aboutissant à la guérison, Bull. Soc. franç. de dermat. et syph. **33**:536, 1926.

75. Stokes, J. H.: Acute Septicemia with Manifestations of Pemphigus, Toxic Myocarditis and Nephritis, Arch. Dermat. & Syph. **36**:405 (Aug.) 1937.

76. Kinnear, J.: Pemphigus: A Review of Seven Cases, Brit. J. Dermat. **50**:236, 1938.

77. Purjesz, S.: Zur Streitfrage über die Existenz des Pemphigus acutus, Deutsches Arch. f. klin. Med. **17**:271, 1876.

78. Spillmann, P.: Contribution à l'histoire du pemphigus aigu, Ann. de dermat. et syph. **2**:66, 1881.

(Footnotes continued on next page)

LABORATORY STUDIES

Bacteriologic studies of the lesions and of the blood have been unsuccessful in establishing an etiologic agent for erythema multiforme.

In cases of severe erythema multiforme anemia may develop within a short time. In most cases recorded in the literature there was a normal leukocyte count or a moderate leukocytosis. Fiessinger and Rendu,[2] Stevens and Johnson [4] and Storck [21] each found, however, leukopenia (counts of 3,800, 4,600 and 4,800 leukocytes, respectively) in 1 case. Differential counts usually have shown a moderate increase in the number of polymorphonuclear cells. Eosinophilia has not been reported, and in some cases eosinophils were absent.

Fanconi,[18] the only author to report an examination of the spinal fluid, found in his patient a mild pleocytosis (14 lymphocytes), an increase of protein (43 Gm. per hundred cubic centimeters) and changes in the colloidal gold curve to 2 3 3 4 2 1 1 1 1.

In the urine small amounts of albumin are common at the height of the disease.

REPORT OF CASES

Case 1.—An American man aged 49 at 2 p. m. on June 30, 1937 experienced slight discomfort in the right side of his throat and began to feel feverish. A few hours later his lips began to swell, and crops of blisters appeared in rapid succession on the mucous membranes of his lips, mouth and throat. Eight hours after the onset of his symptoms he became unable to swallow and experienced difficulty in breathing.

On admission to the hospital, shortly after midnight on July 1, ten hours after the onset of his symptoms, the patient appeared extremely ill. His temperature was 104 F. Numerous bullae and erosions were present on his lips, in his mouth and in his throat extending as far down as the piriform sinuses. The lips, tongue, epiglottis and arytenoid region were swollen. There was considerable salivation, the saliva being tinged with blood. There were no cutaneous or other mucosal lesions. The heart and lungs were normal. In the course of the day a macular and papular eruption appeared on the patient's skin. Most lesions were on the flexor surfaces of his extremities, but a few were present also on his neck, chest and abdomen.

On July 2, the third day of his illness, the patient appeared to be near death. The temperature varied between 102 and 103.8 F. The mouth and throat presented many new bullae and numerous large erosions. The epiglottis was swollen to such a degree that the view of the larynx was obstructed, but increased difficulty in breathing suggested increased edema also of the larynx. The possibility of an immediate tracheotomy had to be considered. The cutaneous eruption had become much more extensive. In many areas, particularly on the extremities, the macular and papular lesions had coalesced into large erythematous patches. There were vesicles and bullae on some of the patches. An erythematous lesion involving more than half of the surface of the glans penis was first noted. The conjunctivas had become injected, and several vesicles and erosions were present in the lower conjunctival fornices.

On the fourth day, the patient appeared to be in a slightly better condition. The temperature varied between 103 and 104.2 F. Only few new bullae were noted on the oral mucosa, and the edema of the pharynx and larynx had decreased. For the first time vesicles and erosions were noted on the nasal mucosa near the nostrils. The patient also complained of severe burning in the anal region, where the mucous membrane had prolapsed and was swollen and eroded. The cutaneous eruption had further extended and was now predominantly bullous. Although a few of the bullae developed on normal-appearing skin, most of them were within areas of erythema. In many of the erythematous areas the upper layer of the epidermis could be rubbed off by pressure of the thumb (positive Nikolsky sign).

During the fifth to the seventh day of his illness the patient had an irregular temperature with a maximum of 104 F. every day. He still appeared seriously ill and prostrate and suffered from hallucinations. The edema of the oral, pharyngeal and laryngeal mucosa decreased further. The cutaneous eruption, however, continued to spread, so that on the seventh day the skin of the extremities, the face, the anterior surface of the neck and the scrotum was nearly covered with either bullous lesions or erosions. The skin of the trunk was less involved, but it still showed numerous scattered erythematous and bullous lesions.

On the eighth day of his illness the patient's general condition was so much better that he could be taken off the danger list. The cutaneous and oral lesions showed definite improvement. The patient began, however, to raise purulent sputum without coughing. Inspection of the larynx revealed ejection of abundant purulent secretion through the glottis, which suggested a purulent tracheitis. After the tenth day no new cutaneous lesions appeared. The temperature gradually fell and from the sixteenth day on never rose above 100 F.

During the third week the cutaneous and oral lesions continued to heal and the prolapsed anal mucosa began to slough. The patient was, however, still dyspneic at times and raised large amounts of purulent sputum. The conjunctivitis continued to be active.

On July 31, the thirty-second day of his illness, the patient was discharged from the hospital. All raw areas in his mouth and on the skin had healed. The sites of former lesions on the skin showed pigmentation. No sputum was raised any more. Only the conjunctivitis was still active and caused considerable photophobia. The conjunctivas appeared slightly edematous, beefy red and partially covered with pseudomembranes. There was a stringy mucoid discharge.

Laboratory Examination.—On the patient's admission to the hospital the number of erythrocytes was 4,800,000 and the number of leukocytes 7,600. The hemoglobin content was 75 per cent (Sahli). A differential count showed 79 per cent polymorphonuclear leukocytes. At the height of the illness, on July 5, the number of erythrocytes was reduced to 3,000,000 and the number of leukocytes to 2,500. The hemoglobin content was 55 per cent. The differential count showed 48 per cent polymorphonuclear leukocytes, 6 per cent of which were myelocytes and 18 per cent stab cells, 36 per cent lymphocytes, 14 per cent monocytes and 2 per cent basophils; there were no eosinophils. A week later, when

79. Danek, F.: Ein Fall von Pemphigus acutus non syphiliticus bei einem Erwachsenen, Wien. med. Wchnschr. **33**:1094, 1883.

80. Robinson, F.: Case of Acute Pemphigus, Brit. M. J. **1**:1033, 1896.

81. Cleveland, D. E. H.: Malignant Pemphigus in a Child, Am. J. Dis. Child. **45**:599 (March) 1933.

the patient was recovering, all values were normal or nearly normal. The eosinophil count remained low and never rose above 1 per cent during the patient's stay in the hospital.

Blood for culture taken on the day of admission showed staphylococci on two occasions. On subsequent days all cultures of the blood were sterile. Smears and cultures from the throat showed gram-positive diplococci, gram-positive diplobacilli and staphylococci. Smears and cultures from the cutaneous blebs showed gram-positive diplococci.

Examination of the urine showed slight traces of albumin at the height of the disease.

Treatment.—Treatment consisted of intravenous infusions of 5 per cent dextrose in isotonic solution of sodium chloride and three blood transfusions.

Further Course.—Two weeks after his discharge from the hospital the patient began to have attacks of hiccups and regurgitation after the eating of solid food. Four weeks after his discharge, he returned to the hospital. A diagnosis of carcinoma of the esophagus was made. This caused his death in October 1937, ten weeks after his first discharge from the hospital. None of the oral or cutaneous lesions had returned, but the conjunctivitis with photophobia had persisted until his death.

CASE 2.—On April 7, 1941 a 35 year old man of French-Canadian descent had a sore throat and a temperature of 102.6 F. The next day he began to cough and to raise frothy white sputum. During the ensuing week the soreness of his throat increased and the sputum became streaked with blood. His temperature ranged around 100 F. On the eighth day of his illness the patient began to feel a sharp pain in the center of his chest whenever he coughed or raised sputum. On the tenth day of his illness, the temperature rose higher, his throat felt so sore that he was unable to swallow and his mouth began to hurt. His eyes also became sore, and he noticed scattered macular lesions on his arms and legs. Since all manifestations rapidly increased in severity, he was sent to the Massachusetts General Hospital on April 18, the twelfth day of his illness.

On admission the patient appeared dangerously ill. His temperature was 104 F. He complained of a severe burning sensation in the center of his chest. He had great difficulty in breathing and incessantly raised large amounts of blood-streaked sputum. Because of severe hoarseness he was unable to speak above a whisper. He was placed on the danger list, and a tracheotomy set was held in readiness. Examination showed large areas of the mucous membranes of the lips and mouth denuded of epithelium. The lips were considerably swollen, and the mouth was filled with blood-streaked saliva and sputum. A few intact vesicles and bullae were present. Examination of the throat revealed considerable edema of the epiglottis, which obstructed the view of the larynx. There was a stringy mucoid discharge from the eyes. The tarsal conjunctivas were edematous, beefy red and partially covered by pseudomembranes. In the lower fornices the conjunctivas had a brownish hue and a rubbery appearance. The corneas were clear. The mucous membranes of the nose showed small erosions and bloody crusts near the nostrils. A large erosion was present on the mucosa of the glans penis. The cutaneous eruption consisted of vesicles and bullae, most of which were on an erythematous base though some were on normal-appearing skin. Most of the lesions were on the extremities, particularly on the hands and feet, but scattered lesions were present also on the face and trunk. Auscultation of the lungs revealed numerous rhonchi throughout both lungs. The breath sounds were bronchovesicular. There was no clinical evidence of massive consolidation. A roentgenogram of throat and chest showed edema of the epiglottis and arytenoid region, thickening of the heavy lower left bronchi and generalized increased marking throughout the chest.

During the following four days the temperature remained between 102 and 103 F. The condition of the patient's mouth, throat and trachea continued to be as severe as on the day of his admission to the hospital. The eyes and skin became worse.

On the seventeenth day of his illness, the sixth of hospitalization, the patient appeared considerably improved. The laryngeal edema had decreased so that he was able to breathe freer. The temperature remained under 101 F. From this day on his mouth, throat, eyes and skin began to improve. Healing, however, was slow, and new bullae, though less in number, continued to appear on the skin as well as on the mucous membranes. The patient continued to expectorate large amounts of sputum. A roentgenogram of the lungs taken on the nineteenth day of illness showed a densely mottled appearance of the lower and middle lobes of the right lung.

On the twenty-third day the temperature rose again to 104 F. and remained at this height until the twenty-ninth day. A bronchiolitis of the lower and middle lobes of the right lung and, to a lesser degree, of the lower lobe of the left lung was believed to be the cause of the fever.

On the thirty-first day a roentgenogram of the lungs showed considerable regression of the dense mottling in the right lung. The patient continued, however, to produce copious amounts of mucopurulent sputum which, because of the absence of physical signs and roentgenographic evidence of involvement of the alveoli, was believed to be caused by inflammation of the mucosa of the trachea and bronchi. The skin, which had shown no new lesions from the twenty-eighth day on, had entirely healed on the forty-sixth day. The oral mucosa, however, continued to show new erosions, and the conjunctivitis remained active.

On June 9, the sixty-fourth day of his illness, the patient was able to leave the hospital. He still coughed frequently and raised copious amounts of thick, tenacious sputum. The skin showed only areas of pigmentation at the site of former lesions. The oral mucosa showed several areas of denudation. The palpebral and bulbar conjunctivas showed diffuse inflammation, and there was evidence of scarring and shrinking with partial obliteration of both lower cul-de-sacs. The corneas showed no ulcerations. The patient had considerable photophobia but no pain. A soft adhesion between the foreskin and the glans penis was present near the frenulum.

Laboratory Examination.—On the patient's admission to the hospital the number of erythrocytes was 4,900,000. The number fell to 3,600,000 on the twenty-sixth day of illness. On his discharge the number of erythrocytes was 4,520,000. The leukocyte count on admission was 22,000. It remained between 10,000 and 20,000 until shortly before his discharge; one week before discharge it was 8,600. Differential counts showed an increase of polymorphonuclear leukocytes to around 80 per cent during the first two weeks of hospitalization, but later values were normal. On his admission no eosinophils were present; subsequent counts ranged from 1 to 4 per cent eosinophils. Chemical examination of the blood on the twenty-second day of illness showed slightly lowered values for calcium (4.6 milliequivalents per liter), sodium (137 milliequivalents per liter) and protein (5.8 Gm. per hundred cubic centimeters). The non-

protein nitrogen content was 20 mg. per hundred cubic centimeters. A phenolsulfonphthalein test performed on the twenty-sixth day of illness showed 77 per cent excretion within one hour.

Repeated cultures of the blood yielded no organisms. A smear of material taken from the palate showed many gram-positive cocci and bacilli, as well as fusiform bacilli and Vincent's spirochetes.

The urine did not contain albumin at any time.

Treatment.—During the first two weeks of hospitalization the patient received daily intravenous infusions of 5 per cent dextrose in isotonic solution of sodium chloride. He also received one blood transfusion of 500 cc. Sulfathiazole was given from the twenty-sixth to the thirty-third day of illness. Its use was discontinued because of the development of a diffuse macular eruption which was thought to be caused by its administration. Sulfathiazole did not seem to influence the course of the disease.

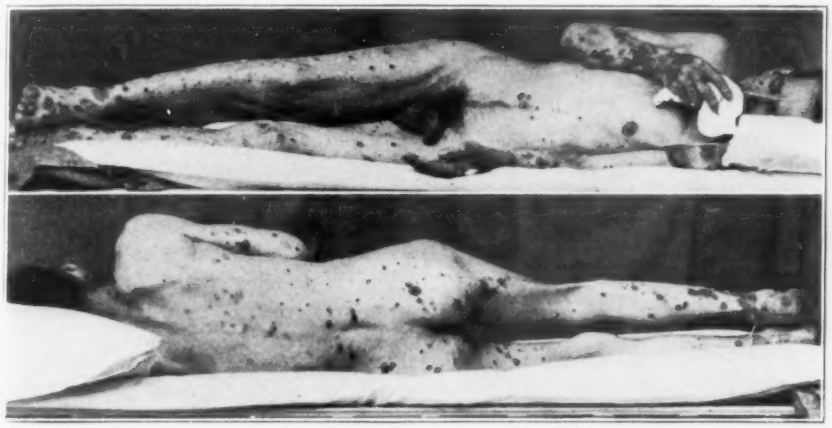
Further Course.—Occasional new lesions continued to form in the oral cavity until four months after onset of the disease. The tracheobronchial symptoms gradually decreased in severity and disappeared five months after onset. The conjunctivitis, however, persisted. The shrinking of the conjunctivas became more severe, and seven months after onset of the disease adhesions between the palpebral and bulbar conjunctivas were first noted. The right cornea began to show superficial ulcers and opacities. In the course of the next few months the entire cornea gradually became affected, so that in the fall of 1942 vision of the right eye was reduced to the perception of shadow and light only. The left cornea remained free from involvement.

On Jan. 10, 1943, twenty-one months after onset of his illness, the patient again suddenly had a high temperature which reached 104 F. the following day. On January 11 numerous vesicles developed on the mucous membranes of the lower lip and the lower gums. A large erosion appeared on the glans penis and about a dozen macular lesions on each forearm. New lesions in small number continued to appear in these areas for about a week. Some of the macular lesions of the skin developed central vesicles. Four weeks after onset of the attack all lesions had healed and, as before, the eyes remained the only active areas.

No appreciable change took place in the eyes during subsequent months, and in August 1943 the vision was of the same acuity as it had been in the fall of 1942.

COMMENT

The 2 cases have in common an acute onset with high temperature. In case 1 the first lesions were in the pharynx and the mouth; in case 2, in the pharynx and trachea. Within a few hours in the first case and within a few days in the second case, the disease reached its height and presented a severe aspect. In both cases there were severe stomatitis, pharyngitis, laryngitis, tracheitis and conjunctivitis, as well as involvement of the nasal mucosa and the glans penis. The skin presented a predominantly bullous eruption which, although generalized, was most pronounced on the extremities. The first case showed, in addition, involvement of the anal mucosa; the second case, involvement of the bronchial and bronchiolar mucosa. In both cases the severe laryngeal edema required preparations for a possible tracheotomy.



Front and back view of a patient with severe erythema multiforme (case 2), showing the distribution of the cutaneous lesions. The photographs were taken on the nineteenth day of the disease, when the patient had already begun to improve. Because of the constant salivation the patient kept a handkerchief before his mouth while the photograph was taken.

The state of acute emergency persisted, however, in both cases for only a few days. It lasted from the first to the fourth day in case 1 and from the twelfth to the seventeenth day in case 2. Thereafter gradual improvement took place. Cutaneous lesions ceased to form in case 1 after ten days of illness and in case 2 after twenty-eight days of illness. On some of the mucous membranes, however, new lesions appeared for a considerably longer time. In case 1 the conjunctivitis continued until the patient's death, which occurred from carcinoma of the esophagus three and a half months after onset of the disease. In case 2 the stomatitis did not heal until four months after onset of the disease

and the bronchitis not until five months after onset of the disease, while the conjunctivitis had remained active up to the time that this report was written, a period of twenty-eight months. In case 2 a short, mild recurrence of cutaneous, oral and penile lesions occurred twenty-one months after onset of the first attack. Because of the severe involvement of many of the mucous membranes these 2 cases of erythema multiforme may be classified as belonging to the cases of the type ectodermosis erosiva pluriorificialis.

The following features are regarded as of particular interest in the 2 reported cases: the persistence of the conjunctivitis in both cases, with development of conjunctival scarring and corneal opacities in case 2; the occurrence of an adhesion between the prepuce and the glans penis in case 2; the severe involvement of the anal mucosa in case 1, causing a prolapse of the anal mucosa and subsequent sloughing, and the tracheobronchial involvement which was observed in both cases. In the first patient a tracheitis developed in the second week of illness, after the most acute stage of the disease had already been passed. In the second patient tracheitis was an early symptom which was soon followed by bronchitis and bronchiolitis. In regard to the laboratory studies, it is of interest that in case 1 the number of erythrocytes fell from 4,800,000 to 3,000,000 within four days; in case 2, from 4,900,000 to 3,600,000 within sixteen days. In case 1 the leukocyte count fell to 2,500 on the sixth day of illness.

Both patients were carefully questioned in regard to their intake of drugs. The first patient had occasionally taken a laxative containing phenolphthalein. He had taken none, however, during the two weeks preceding his illness. The second patient said that he had not taken any drugs for several months before his illness.

SUMMARY

Severe erythema multiforme starts abruptly with high fever and severe constitutional symptoms. An extensive predominantly bullous eruption of the skin and mucous membranes develops within a few days. The oral, pharyngeal, laryngeal, tracheal, bronchial, nasal and anal mucous membranes, the conjunctivas and the glans penis may be involved. In spite of the severe clinical picture at the onset, a fatal outcome is rare. Improvement usually begins within a few days, and after a few weeks the patient has recovered, usually without residual damage. The only area where permanent damage may result is the eyes. Occasionally the conjunctivitis if severe may lead to keratitis, iritis and panophthalmitis, or the conjunctivitis may become chronic and result in cicatricial contraction of the conjunctivas.

The number of cases of severe erythema multiforme reported in the literature is not large. In many cases the disease was not recognized as such. Diagnostic terms such as *ectodermose érosive pluriorificielle,* "dermatostomatitis" and "eruptive fever with stomatitis and ophthalmia" have been used. It is believed that in addition, some of the cases reported as pemphigus acutus were in reality cases of severe erythema multiforme. On the other hand, the severe and often fatal eruptions with visceral complications reported by Osler and others as erythema multiforme are not regarded as that disease.

The 2 patients with severe erythema multiforme reported on in this communication were dangerously ill when admitted to the hospital. Involvement of the laryngeal and tracheal mucosa produced alarming symptoms of dyspnea, which required preparations for immediate tracheotomy. In both cases improvement began within a few days, and after a few weeks all lesions had healed except those of the conjunctivas. They persisted in case 1 until death from carcinoma of the esophagus occurred two and a half months after the patient's discharge from the hospital and have persisted in case 2 up to the time of writing, a period of over two years. In this case scarring of the conjunctivas and of the right cornea developed.

RELATIONSHIP OF BALANITIS XEROTICA OBLITERANS TO LICHEN SCLEROSUS ET ATROPHICUS

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In 1941, we [1] reported observations based on a study of 18 cases of balanitis xerotica obliterans, a disease of the male genitals to which attention was first called by Stühmer [2] in 1928. Balanitis xerotica obliterans may be briefly defined as a chronic, progressive, atrophic, sclerosing process of the glans and prepuce leading to urethral stenosis. Operations on the genitals, such as circumcision and dorsal incision, are not etiologic factors in our opinion. In contradistinction to Stühmer's [2] belief that the disease occurs only in young adults, we feel that it may occur at any age.

The onset of balanitis xerotica obliterans is as a rule insidious, although it may appear as an acute disease with pain, itching, burning, prickling and profuse purulent secretion. It becomes chronic and in most cases slowly progressive up to a certain point, where it remains stationary. In patients who have not been circumcised there is an almost constant involvement of the prepuce in the form of a sclerotic, constricting band which is located 1 or 2 cm. from the distal end. The involvement of the glans may be diffuse or as mottled patches. The admixture of the white plaques and normal red tissue of the glans may give rise to a mosaic appearance, and if telangiectasia is present there may be a resemblance to roentgen ray dermatitis. Fissures and erosions are rather common, and hemorrhagic or serous bullae often accompany the cicatricial changes. The eventual development of carcinoma was reported by Stühmer, Frühwald [3] and Grütz.[4] One of the most noteworthy features of balanitis xerotica obliterans is the gradual narrowing of the urethral meatus, which often leads to almost complete stricture.

The association of balanitis xerotica obliterans and lichen sclerosus et atrophicus was not noted in any of our 18 patients discussed in 1941, although unfortunately we made no careful search for lesions elsewhere on the body. Unless such an examination were made, it would be easy to overlook small papules or patches of lichen sclerosus et atrophicus on the body when attention was focused on the genital lesions which were causing urethral stenosis with resulting disturbances in urination. Our attention was called to a possible relationship between the two diseases in 1940 at a meeting of the Minnesota Dermatological Society, where Dr. Fred Becker presented a patient with unmistakable papules of lichen sclerosus et atrophicus in the clavicular and scapular regions and on the shaft of the penis and scrotum, along with characteristic sclerosing lesions of balanitis xerotica obliterans on the prepuce and glans. It was impossible to obtain a specimen for biopsy from the glans, although the histologic structure of a lesion from the clavicular region was that of lichen sclerosus et atrophicus.

Fabry [5] in 1928 reported a case in which there was in all probability a similar association. The patient, aged 35, was said to have had "kraurosis penis" and "white spot disease" on the scrotum. Judging from the photomicrograph in the article, we believe that the eruption on the scrotum was lichen sclerosus et atrophicus.

Montgomery and Hill [6] presented an excellent study of lichen sclerosus et atrophicus in 1940. In their group of 46 patients the disease occurred in 8 males, only 1 of whom had penile lesions. In this case there were characteristic papules of lichen sclerosus et atrophicus on the shaft but no sclerosing atrophic lesions on the glans and prepuce such as characterize balanitis xerotica obliterans.

Since our previous report we have carefully examined 6 additional patients with balanitis xerotica obliterans. One of these presented no lesions of interest elsewhere on the body. Another showed multiple striae and atrophic scars on the

From the Division of Dermatology, University of Minnesota, H. E. Michelson, M.D., Director.

1. Freeman, C., and Laymon, C. W.: Balanitis Xerotica Obliterans, Arch. Dermat. & Syph. **44**:547 (Oct.) 1941.

2. Stühmer, A.: Balanitis xerotica obliterans (postoperationem) und ihre Beziehungen zur "Kraurosis glandis et praeputii penis," Arch. f. Dermat. u. Syph. **156**:613, 1928; Weitere Beiträge zur Kenntnis der Balanitis xerotica obliterans post operationem, ibid. **165**:343, 1932.

3. Frühwald: Peniscarcinom nach Balanitis xerotica obliterans (Stühmer), Zentralbl. f. Haut- u. Geschlechtskr. **50**:98, 1935.

4. Grütz, O.: Beiträge zur Klinik der Balanitis xerotica obliterans, Dermat. Wchnschr. **105**:1206, 1937.

5. Fabry, J.: Ueber einen Fall von Kraurosis penis bei gleichzeitigem Bestehen von Weissflecken am Skrotum, Dermat. Wchnschr. **86**:7, 1928.

6. Montgomery, H., and Hill, W.: Lichen Sclerosus et Atrophicus, Arch. Dermat. & Syph. **42**:755 (Nov.) 1940.

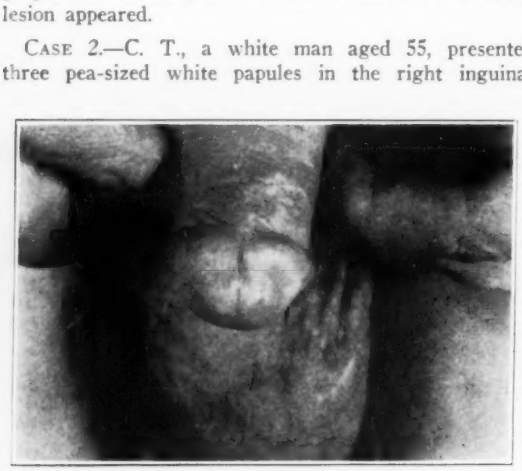
body (said to have followed furunculosis), some of which bore a close resemblance to patches of lichen sclerosus et atrophicus. The cases of the other 4 patients are briefly summarized.

REPORT OF CASES

CASE 1.—H. L., a white man aged 25, had three typical plaques of lichen sclerosus et atrophicus on the back, the largest (3 cm. in diameter) in the midline just below the collar line and a smaller lesion (1 cm. in diameter) to either side and below the largest one. The largest one appeared in 1933. There was a similar patch 4 by 2 cm. in the right clavicular region which presented follicular dilatation and plugging. The lesion was noted first in 1939. Several isolated achromatic papules were seen in the left clavicular region.

There were shiny white atrophic patches on the glans and a constricting ring about the prepuce; the frenulum was sclerotic, and the urethral meatus was slightly but definitely narrowed. Tightness of the prepuce was noted at the same time the clavicular lesion appeared.

CASE 2.—C. T., a white man aged 55, presented three pea-sized white papules in the right inguinal



White sclerotic plaques on the glans, urethral narrowing and constriction of the retracted prepuce (case 1).

region which were typical of lichen sclerosus et atrophicus. In addition, there were distinct urethral stenosis and patchy involvement of the glans which were identical with those of all of our other patients with balanitis xerotica obliterans. No histologic studies were made.

CASE 3.—C. D., a white man aged 37, presented a sclerotic band about the prepuce of a year's duration, definite narrowing of the meatus with difficulty in urination, atrophic plaques on the glans and several white shiny papules over the scapulas which showed well developed follicular plugging. Biopsy was not permitted.

CASE 4.—J. P., a white man aged 67, noted difficulty in retracting the prepuce during the summer of 1942. When he was examined in February 1943 there was a constricting band of sclerotic tissue about the prepuce and white patches on the glans but only slight narrowing of the meatus. All along the shaft and extending down to the preputial constriction were white papules such as are seen with lichen sclerosus et atrophicus. There were no other lesions elsewhere on the body. The patient was circumcised, and the tissue which was removed included isolated papules and the constricting band, which were in approximation.

COMMENT

In our previous report on balanitis xerotica obliterans we speculated briefly concerning its relationship to lichen sclerosus et atrophicus. The primary lesion of the latter disease is a flat, irregular, often polygonal papule of the color of ivory or mother of pearl. The papules may remain discrete, or they may coalesce to form plaques; in most cases both types of lesions are present. The presence of cells and follicular plugs aids in the diagnosis. The article of Montgomery and Hill contains an excellent photograph of multiple discrete papules on the shaft of the penis in lichen sclerosus et atrophicus. One of our patients (case 4) had practically identical lesions plus constricting involvement of the prepuce, plaques on the glans and narrowing of the meatus. The histologic features were entirely consistent with those regarded as characteristic of lichen sclerosus et atrophicus, and, since the patient was circumcised, the opportunity was afforded to compare the histologic features of the isolated papules with those of the constricting band, all in one section. They appeared identical.

It is not our purpose here to discuss the possible relation of lichen planus to lichen sclerosus et atrophicus, although we share the views of Nomland [7] and Montgomery and Hill [6] that the two are separate entities. In our 24 cases of balanitis xerotica obliterans we never saw associated lichen planus.

We previously stated our opinion that so-called kraurosis penis and balanitis xerotica obliterans are identical, and there is no need to repeat here our reasons for this view. Briefly, however, there are no essential differences in either the clinical or the histologic features. It is beside the point also in this paper to open discussion as to whether balanitis xerotica obliterans (kraurosis penis) is the analog in the male of kraurosis vulvae. Certainly there is considerable difference of opinion concerning the relationship of kraurosis vulvae to lichen sclerosus et atrophicus affecting the female genitals. We plan to make this the subject of future investigation.

For fully developed balanitis xerotica obliterans it is possible to make a definite histologic diagnosis. The epidermis is distinctly atrophic, with relative and absolute hyperkeratosis. There may be a moderate degree of intracellular edema in the lower portions of the epidermis and slight

7. Nomland, R.: Lichen Sclerosus et Atrophicus (Hallopeau) and Related Cutaneous Atrophies, Arch. Dermat. & Syph. **21**:575 (April) 1930.

liquefaction degeneration of the basal layer, beneath which there may be a few lymphocytes. The most striking histologic feature is the band of homogenized connective tissue in the upper portion of the cutis. This zone appears relatively acellular and edematous and may show diminution or complete disappearance of the elastic tissue. We have also seen a bandlike infiltration beneath the homogenized zone in one of our later patients showing the clinical features of balanitis xerotica obliterans and presenting patches of lichen sclerosus et atrophicus on the body (case 1). It is immediately obvious to dermatopathologists that the aforementioned histologic description of balanitis xerotica obliterans could just as well be used to characterize lichen sclerosus et atrophicus, since the features of both are identical. In case 1 biopsies were performed on specimens from the clinical lesions of lichen sclerosus et atrophicus on the body as well as from the plaques on the genitals regarded as balanitis xerotica obliterans, and there were no noteworthy differences in the conditions observed.

In case 2 the genital lesions were in every way characteristic of balanitis xerotica obliterans. The lesion in the groin was just as typical of lichen sclerosus et atrophicus, and it is especially interesting that the patient had been seen previously by other dermatologists and that they had expressed the opinion that the disease was lichen sclerosus et atrophicus.

In case 3, although histologic studies were not permitted, the same association was noted clinically.

We are of the opinion, then, that balanitis xerotica obliterans and lichen sclerosus et atrophicus are identical. Lichen sclerosus et atrophicus can occur on the male genitals in two forms: (1) as isolated papules on the shaft and (2) as a constricting band about the prepuce, with plaques on the glans and urethral stenosis. Both forms may coexist, and both may occur alone or with ordinary lesions of lichen sclerosus et atrophicus elsewhere on the body. The histologic features of all types of lichen sclerosus et atrophicus are, as should be expected, the same.

SUMMARY AND CONCLUSIONS

Six cases of balanitis xerotica obliterans are added to the 18 previously reported. Four of the patients had plaques of lichen sclerosus et atrophicus on the body in association with the genital lesions, and another showed typical isolated papules of lichen sclerosus et atrophicus on the shaft of the penis with lesions of balanitis xerotica obliterans on the glans and prepuce.

In our opinion lichen sclerosus et atrophicus and balanitis xerotica obliterans are identical.

Lichen sclerosus et atrophicus may occur on the genitals as (1) isolated papules on the shaft or (2) sclerotic preputial and urethral involvement, with patches on the glans. Both types of genital involvement may occur alone or with lesions on the body. All forms present the same histologic features.

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Clinical Notes

REPLACEMENT GRAFT IN SURGICAL TREATMENT OF LUPUS VULGARIS

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In a previous communication [1] we stated that the best treatment of lupus vulgaris in many instances is excision and that the limitation of this procedure is of technical nature dealing with the repair of the wound occasioned by it. The advantages of this therapeutic approach include the great likelihood of quick and complete eradication of the disease, the avoidance of unsightly unhealthy scarring and the circumvention of long, tedious, expensive and frequently inadequate treatment. All of these considerations justify the assumption of the hazards offered by surgical intervention and the difficulties of repair which may be occasioned.

The following report of a case underlines these contentions.

REPORT OF A CASE

Mrs. I. G., a 47 year old housewife of Scottish parentage, was referred to the Pittsburgh Skin and Cancer Foundation by Dr. R. M. Smith on March 12, 1942, on account of a well defined nodular scaly plaque of a peculiar dusky red color covering the central portion of the upper lip. It extended from the line of the anterior nares to and involving the vermilion border of the lip. It measured 2.5 cm. at its widest diameter. This plaque began as a small nodule one year previously and slowly enlarged in spite of a variety of topical medication.

In the central portion of the left cheek and approximating the nasolabial fold an extensive flat whitish scar was present. It was the result of a similar eruption destroyed by electrodesiccation twelve years previously.

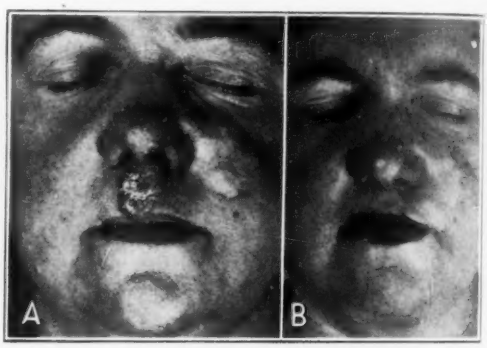
The previous medical history was unimportant except that at the age of 29 an enlarged tuberculous lymph node was removed from the left cervical area, the scar of which was still evident. The patient has been married for twenty-six years and has one living and healthy child.

The diagnosis of lupus vulgaris (later confirmed by microscopic examination) was made by the presence of the pathognomonic apple jelly nodules.

General examination, including a careful examination of the chest, revealed conditions that were normal in all respects. This was true of the serologic investigation also. A number of blood counts showed that the composition of the blood was within normal limits. A tuberculin patch test (Vollmer) elicited a strongly positive reaction.

Treatment.—Thirty intravenous injections of gold sodium thiosulfate were given at weekly intervals. Fifteen of these were 25 mg. and fifteen were 50 mg. doses. As no improvement followed, she was given two intramuscular injections of liver extract each week for a period of fifteen weeks. Then, because no improvement followed this either, a fifteen week course of injections of bismuth sodium tartrate was carried out. This was equally ineffectual. Thus, a period of fourteen months elapsed without any benefit from this tedious, at times painful and at times inconvenient treatment.

On May 18, 1943, the lupus vulgaris–bearing area was excised under local anesthesia, and a free graft obtained from the submental area was applied over the wide gaping wound. The free graft was sewed into place with interrupted and closely placed silk sutures. In addition to these marginal sutures, however, a through and through heavy silk suture was placed through the middle portion of the free graft. This suture embraced the entire thickness of the lip, and the pressure thus occasioned on the graft enhanced the possibility of the "take" of the under surface as well as at the margins. This minor technical provision proved to be of utmost importance.



A, the original lupus vulgaris; *B*, the appearance six weeks after excision and free grafting.

The further course was uneventful. The graft adhered; all of the sutures and dressings were removed after fourteen days, and thus a long and tedious treatment was ended. (Microscopic examination of the excised tissue proved the lesion to be lupus vulgaris.)

CONCLUSIONS

A case report is presented to prove that even in the presence of certain technical hazards replacement grafts offer the quickest, surest and least cumbersome method of treatment in selected cases of lupus vulgaris.

631 Jenkins Buildings, Pittsburgh.

6 South Main Street, Washington, Pa.

From the Pittsburgh Skin and Cancer Foundation.

1. Hollander, L., and Shelton, J. M.: Replacement Grafts in Surgical Treatment of Lupus Vulgaris, Arch. Dermat. & Syph. **40**:263-267 (Aug.) 1939.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

THE RESULTS OF A TWENTY-WEEK TREATMENT SCHEDULE FOR EARLY SYPHILIS. B. J. HOOD, Am. J. Syph., Gonor. & Ven. Dis. **27**:267 (May) 1943.

A short treatment schedule was followed in treating early infectious syphilis, concomitant weekly injections of mapharsen and bismuth being given for twenty weeks.

Ninety-four and four-tenths per cent of all primary and secondary manifestations of syphilis had undergone involution within six weeks. A rapid and satisfactory fall of reagin to negative occurred in 84.8 per cent of the patients completing treatment. During the follow-up period this figure was further raised to 90.9 per cent through spontaneous attainment of seronegativity without treatment in patients whose reactions were seropositive at the conclusion of the twenty weeks' course. In general, the flocculation reactions (Eagle, Kahn) remained positive for an average of two weeks after the Wassermann reaction (Kolmer) first became negative.

Seroresistance, serorelapse, clinical relapse and involvement of the central nervous system accounted for a total of 13.6 per cent unsatisfactory results in clinical and serologic follow-up for a period of one to thirty-three months. This compares not unfavorably with the expected unsatisfactory results obtained in patients with early syphilis treated with other arsenical drugs and other systems of treatment.

POSTARSPHENAMINE LICHEN PLANUS. M. H. GOODMAN and R. W. RECKLING, Am. J. Syph., Gonor. & Ven. Dis. **27**:280 (May) 1943.

The problems involved in the elucidation of the lichen-planus-like eruptions which develop in the course of antisyphilitic therapy with the arsphenamines are discussed.

Studies previously made seem to indicate that the usual type of postarsphenamine lichenoid eruption, commonly designated as the lichen-planus-like exanthem, is microscopically distinguishable from true lichen planus, as exemplified by the eruption in the authors' case, and is a lichenoid toxic erythema.

A NOTE ON THE CULTIVATION OF TREPONEMA PALLIDUM WITH THE PRESERVATION OF VIRULENCE. C. C. KAST and J. A. KOLMER, Am. J. Syph., Gonor. & Ven. Dis. **27**:309 (May) 1943.

All attempts to cultivate Treponema pallidum (Nichols-Hough strain) in a medium prepared of normal rabbit testicular tissue after the method of Morrison were completely unsuccessful.

The cultivation of T. pallidum with preservation of virulence for rabbits is still an unsolved problem.

CARDIOVASCULAR INVOLVEMENT IN CONGENITAL SYPHILIS. J. HINRICHSEN, Am. J. Syph., Gonor. & Ven. Dis. **27**:319 (May) 1943.

From an exhaustive review of the literature it is concluded that congenital syphilis produces myocardial lesions of two types, namely interstitial and nodular myocarditis, in which spirochetes can be demonstrated. No evidence could be found that congenital syphilis produces valvular cardiac lesions. The role of this disease in the production of aortitis and aneurysm and in the production of congenital malformation of the heart has not been determined definitely. Syphilitic arteritis, particularly cerebral arteritis, may be produced by congenital syphilis. It is possible that congenital syphilis is a factor in the production of arteriosclerosis and of Raynaud's disease. Congenital syphilis is one of the causes of hemorrhagic disease of the newborn.

PRIMARY GONORRHEAL CUTANEOUS INFECTION. E. C. LOWRY and A. G. FRANKS, Am. J. Syph., Gonor. & Ven. Dis. **27**:428 (July) 1943.

In the case reported, gonorrheal infection occurred by direct inoculation of the cutaneous surface of the shaft of the penis with gonococci. The eruption consisted of several discrete lesions which appeared as excoriated or ruptured pustules with surrounding erythema and resembled small furuncles. Gonococci in pure culture were isolated from a pustule. There was no evidence of urethral irritation or discharge. The usual routine treatment was ineffective, cure being finally accomplished by destruction of the lesions by electrocoagulation.

THE EFFECT OF PROLONGED TRYPARSAMIDE THERAPY UPON LIVER FUNCTION. I. KOPP and H. C. SOLOMON, Am. J. Syph., Gonor. & Ven. Dis. **27**:445 (July) 1943.

Kopp and Solomon report the results of a series of studies of hepatic function on a group of patients to the majority of whom one hundred or more injections of tryparsamide had been administered. Tryparsamide causes relatively little damage to the liver even when given over a prolonged period and combined with fever therapy.

Jaundice occurring during therapy with trivalent or pentavalent arsenicals, with fever or with a combination of the two disappears without important damage to the liver and is in itself no contraindication to the further use of tryparsamide.

Malarial fever produces evidence of hepatic damage which is transient. The use of tryparsamide immediately after fever treatment does not increase the amount of damage or delay repair.

THE PROBLEM OF TREATMENT-RESISTANT SYPHILIS. H. BEERMAN, N. R. INGRAHAM and H. PARISER, Am. J. Syph., Gonor. & Ven. Dis. **27**:460 (July) 1943.

Previous studies have suggested that the host plays a prominent role in arsphenamine-resistant syphilis, either because of his inability to form an "avid," or active, form of the arsenical or because of his production of a protein combination which is nonspirocheticidal. Arsenoxide is thought to be the active form to which arsphenamine is reduced in the body, and the use of this compound in a case of arsphenamine-resistant syphilis should theoretically be an ideal method to determine whether or not the host can produce the active form of the drug and, if not, thus be responsible for the resistance to arsphenamine. Previous reports, however, have shown that resistance to mapharsen does occur.

Arsenoxide (mapharsen) was given to 7 patients whose infections resisted other arsenical drugs. In 3

patients it overcame the resistance, but in 3 other cases the infection failed to respond to the drug. In 1 case the effect of the drug could not be determined.

These results led the authors to conclude that mapharsen (arsenoxide) is not the active arsenical derivative but that it acts in cases of treatment-resistant syphilis in the same manner as other arsenicals substituted for an arsenical to which the patient's syphilis is resistant.

THE ORAL ADMINISTRATION OF MAPHARSEN IN THE TREATMENT OF EXPERIMENTAL SYPHILIS OF RABBITS. H. BROWN, J. A. KOLMER and A. M. RULE, Am. J. Syph., Gonor. & Ven. Dis. **27**:480 (July) 1943.

The total minimal curative dose of mapharsen by oral administration was at least ten times higher than the single minimal curative dose by intravenous injection and three to four times higher than the single minimal curative dose by intramuscular injection (in sterile peanut oil), while the total minimal curative doses of arsphenamine and neoarsphenamine by oral administration were about eight times higher than by intravenous injection.

In terms of arsenic administered, however, the therapeutic effectiveness of mapharsen by oral administration is higher than that of arsphenamine and of neoarsphenamine.

On the basis of the urinary excretion of arsenic in rabbits it appears that mapharsen is as readily absorbed from the gastrointestinal tract as arsphenamine and neoarsphenamine.

THE TOXICITY AND THERAPEUTIC EFFECTIVENESS OF MAPHARSEN BY INTRAMUSCULAR ADMINISTRATION. H. BROWN, J. A. KOLMER and A. M. RULE, Am. J. Syph., Gonor. & Ven. Dis. **27**:488 (July) 1943.

In view of the much lower toxicity of mapharsen in peanut oil by intramuscular injection than of aqueous solutions by intravenous administration and in view of its rapid absorption and high therapeutic effectiveness by the former route, the authors suggest that intramuscular injection of the compound, including five daily injections of 0.24 Gm. each in the massive arsenotherapy of syphilis in its early stages, may prove of value in the treatment of the disease.

REUTER, Milwaukee.

PINTA (MAL DEL PINTO, CARATE) IN CONTINENTAL UNITED STATES. E. P. LIEBERTHAL, J. A. M. A. **123**:619 (Nov. 6) 1943.

Pinta is a nonvenereal type of spirochetosis limited almost exclusively to the dark races. The initial lesion appears on the cutaneous surface at the exact site of entrance of the causative organism, Treponema carateum, after an incubation period of seven to twenty days. In five months to a year the secondary lesions, or pintids, appear. These are disseminated pink, red, slate blue, brown or black macules and plaques, grouped around the primary lesions. They may be associated with erythema, follicular keratosis and palmar and plantar keratoses. In the terminal stage achromic and hyperpigmented spots and atrophy of the skin are encountered. In this stage the Wassermann and Kahn reactions are strongly positive. Adenopathy, hypertension, juxta-articular nodules, cardiovascular lesions and changes in the spinal fluid are other possible late manifestations.

Diffuse or punctate palmar and plantar hyperkeratoses with or without fissures, which are characteristic of Cuban pinta, are absent in the Mexican form.

The treatment of pinta is similar to that of syphilis. Lieberthal reports on 3 patients whom he observed in a Chicago dermatologic clinic. The patients maintained that they had never had sexual relations or shared living quarters with persons who had lived in the tropics or who had had lesions resembling theirs. The subjects of this report were born respectively in Canada, Louisiana and Alabama.

Although the occurrence of pinta has never before been reported in the continental United States, there are probably persons with the disease in the southern part of the country.

HENSCHEL, Denver.

ALLERGY TO FOOD ODORS: ITS RELATION TO THE MANAGEMENT OF INFANTILE ECZEMA. ARTHUR J. HORESH, J. Allergy **14**:335 (May) 1943.

The author reports a series of 9 cases of atopic eczema in which exacerbations were provoked by inhalation of vapors or odors from foods, either cooked or raw. The skin of every patient remained clear when proper precautions were taken.

Eight patients were infants 7 months to 20 months old; 1 patient was 13 years old.

The offending foods included raw egg, fried fish, fried pork, fried bacon, cooked cabbage and fully dressed chicken. In every case a scratch test with the offending food elicited a 2 to 4 plus reaction.

MENDELSOHN, New York.

HYPOTHERMIA IN EXPERIMENTAL INFECTIONS: II. THE EFFECT OF HYPOTHERMIA ON TUBERCULIN SENSITIVITY IN GUINEA PIGS. D. R. DUERSCHNER, CARL MUSCHENHEIM and JAMES D. HARDY, J. Infect. Dis. **72**:183 (May-June) 1943.

It has been a common clinical observation that the degree of reaction to tuberculin in sensitized persons undergoes fluctuation. Fluctuation in the degree of hypersensitiveness to tuberculin injected intracutaneously has also been noted in animals experimentally infected. The causes of the fluctuations have not been determined, although both in human beings and in animals a complete loss of capacity for cutaneous reaction has been frequently associated with overwhelming or terminal tuberculous infection.

The authors undertook experiments to determine the effect, if any, of induced hypothermia on the course of experimental tuberculosis in guinea pigs. They found that repeated reduction of body temperature to levels 4 to 8 degrees (C.) below normal for twenty-four hours at biweekly intervals over a period of six weeks caused no apparent inhibitory or significant promoting effect on experimental tuberculosis in guinea pigs infected subcutaneously with a standard strain of virulent human tubercle bacilli. There was, however, in most instances a delay in the appearance of cutaneous sensitivity to tuberculin in animals so treated and a lessened degree of sensitivity, at least during the period of intermittent treatment. The effect on tuberculin reactions is not due, the authors think, to local cooling of the skin, since the tests were made in the intervals between hypothermic treatments. The reduction in cutaneous sensitiveness differs from any hitherto produced experimentally in that it is unrelated to specific desensitization or to terminal overwhelming infection.

THE EFFECT OF ACTINOMYCIN, CLAVACIN, AND TYROTHRICIN ON STAPHYLOCOCCAL TOXIN. JOHN E. BLAIR and FRANCES A. HALLMAN, J. Infect. Dis. **72**:246 (May-June) 1943.

The current interest in bacteriostatic and bactericidal properties of substances of microbial origin suggests

the problem of their effects on bacterial toxins. The authors thought it advisable to investigate the action of these antibacterial substances on staphylococcus toxin and on the coagulase reaction. Three substances of microbial origin were studied: actinomycin, clavacin and tyrothricin.

They found that actinomycin, clavacin and tyrothricin do not destroy staphylococcus toxin; they do not enhance its hemolytic or lethal action, and they do not prevent its production under favorable conditions in vitro. When staphylococcus toxin is diluted in broth or in solution of sodium chloride and stored for several days at 37 C. or at 4 C., it undergoes a progressive deterioration, which is not prevented by actinomycin, clavacin or tyrothricin. These three microbial substances inhibit the coagulation of rabbit plasma by staphylococci temporarily but not indefinitely. They do not prevent the coagulation of rabbit plasma by sterile filtrates of broth cultures of staphylococci. Actinomycin and clavacin do not inhibit the neutralization of staphylococcus hemotoxin by antitoxin. While tyrothricin appears to prevent the neutralization of hemotoxin, it does not inhibit in mice the protective action of antitoxin against the intravenous injection of a lethal dose of toxin.

CORNBLEET, Chicago.

THE USE OF DALIBOUR'S WATER IN THE TREATMENT OF SKIN DISEASES. G. E. MORRIS, New England J. Med. **229**:509, 1943.

Morris stresses the value of the copper-zinc-camphor mixture (widely used in Europe but not so much as deserved in the United States) as wet dressings, as an ingredient of ointments and creams and as an astringent in powder form and in a deodorant and disinfectant bath. Practical formulas for its use are given.

DALIBOUR'S WATER: ITS USES IN DERMATOLOGY. T. J. RIORDAN, O. CANIZARES and G. E. MORRIS, New York State J. Med. **42**:802 (April 15) 1942.

Dalibour, or D'Alibour, water is a solution of copper and zinc sulfate in camphorated water, widely used in Europe but not so much in the United States, where solution of aluminum acetate N. F. (Burow's solution) is evidently preferred. Properly diluted it is good against many pyodermic infections, acting as a mild antiseptic and astringent and if used in ice cold compresses as an effective antipruritic agent. The safranine gives the solution a pinkish color. However, this ingredient of the classic formula does not seem to have any other value. The solution diluted 1 to 20 used by the authors is probably the weak, or original, formula. They have employed it successfully in over 400 cases of various pyogenic diseases, and they believe that its use should be more widespread.

THE EXTERNAL USE OF 30 TO 50 PER CENT SULFUR IN PETROLATUM IN VARIOUS DERMATOSES. E. W. ABRAMOWITZ, New York State J. Med. **43**:746 (April 15) 1943.

Abramowitz stresses the value of precipitated sulfur in high concentration in white or yellow petrolatum in treatment of many dermatoses when soothing mixtures have failed. It is recommended for severe pityriasis rosea, for eczematous and seborrheic dermatitis, for erythroderma psoriaticum and for rosacea. It is not advised in the treatment of acne vulgaris, neurodermatitis, lupus erythematosus or lichen planus.

The reasons why high concentrations are better tolerated or give less extensive reactions to patch tests than low ones is not clear.

REDUCED TEMPERATURE TREATMENTS FOR BURNS AND FROST-BITE. F. M. ALLEN, L. W. CROSSMAN and F. K. SAFFORD, New York State J. Med. **43**:951 (May 15) 1943.

In 4 cases of severe burns, pain and edema were almost completely controlled by treatment with reduced temperature (ice bags and electric-refrigerated boxes at 50 F.). Refrigeration seems to produce a better scar.

VITAMINS FOR GRAY HAIR. J. J. ELLER and L. A. DIAZ, New York State J. Med. **43**:1331 (July 15) 1943.

Eller and Diaz treated with paraaminobenzoic acid (100 mg. three or four times a day for periods ranging from three to five months) 88 persons of different ages and sexes in various stages of achromotrichia. In only 1 case has there been a definite darkening of all the hair of the scalp and mustache. Consequently they consider that this method of treatment needs further investigation before it is offered to the public as a "cure" for gray hair.

THE DANGER OF CUTANEOUS REACTION TO SULFONAMIDES: REPORT OF TWO CASES OF BULLOUS ERUPTION FOLLOWING THE USE OF SULFANILAMIDE, ONE OF WHICH RESEMBLED PEMPHIGUS VULGARIS. D. BLOOM, New York State J. Med. **43**:1499 (Aug. 15) 1943.

Eruptions due to sulfonamide compounds are produced by primarily toxic effects due to weakness in the cells or in the detoxifying mechanism of the subject, by acquired hypersensitivity of the skin and by the so-called allergotoxic mechanism, a combination of toxic and allergic effects. The eruption most frequently observed is the maculopapular, or morbilliform, type. The other types are scarlatiniform, erythema-multiforme-like, purpuric, varioliform, vesicular, pustular, bullous, exfoliative and pemphigus-foliaceus-like.

Cutaneous reactions are most frequently produced by sulfathiazole and less frequently by sulfadiazine. Sensitization of the skin and other organs takes place not only after oral administration but after local external applications in the form of ointments. Consequently these drugs should not be used in treatment of minor diseases, for if the patient should become sensitized it will be impossible for him to obtain benefit from the drugs at some future time when he may be seriously ill.

Two cases of bullous eruption from sulfanilamide are reported.

An editorial in the same issue of the journal warns against the rapidly growing medical use of sulfonamide compounds in powders, ointments and solutions for superficial and for deep wounds, because of the possibility of contamination with pathogenic organisms not affected by the sulfonamide drug. It includes a resolution of the Section on Dermatology of the Medical Society of the State of New York strongly disapproving the indiscriminate use of sulfonamide drugs for relatively harmless diseases of the skin and condemning the use of prepared dressings containing sulfanilamide which are sold to the laity.

RONCHESE, Providence, R. I.

NOTES ON TREATMENT OF RESPIRATOR DERMATITIS. E. COLIN JONES, Brit. M. J. **1**:757 (June 19) 1943.

Jones compares two methods of treatment of respirator dermatitis. The first 13 patients used calamine lotion and liniment solution of aluminum acetate and various creams, such as 1 per cent ichthammol in zinc oxide cream. This form of treatment was unsatisfactory.

The next 12 patients were given a lint mask soaked in isotonic solution of sodium chloride which was applied to the face areas continuously. When the weeping areas became epithelized, either zinc oxide cream or 1 per cent ichthammol paste was applied.

The latter method of treatment produced prompt healing.

CUTANEOUS HYPERSENSITIVITY TO SULPHONAMIDES. R. G. PARK, Brit. M. J. **2**:69 (July 17) 1943.

Twelve cases are reported in which local application of a sulfonamide compound caused a sensitization dermatitis. When such sensitization has taken place dermatitis can be caused by local application or internal administrations not only of the drug originally used but by other sulfonamide compounds.

The reaction is proportional to the dose of the drug and to the degree of sensitivity. The reaction to oral administration is more sensitive than that to local application, and the reaction on the skin is usually most severe where the original sensitizing applications were made.

It is not known how long this sensitivity persists, but in the cases reported the patients have reacted for periods up to three months after local use of the sulfonamide compound had been stopped.

Intradermal tests with a 1 per cent solution elicited a positive reaction in 4 of 10 subjects tested, while in 10 controlled subjects the reactions were negative. Scratch tests produced no positive reactions. In most of the reported cases the sulfonamide compounds were applied for prolonged periods; patients who were treated for only a few days escaped sensitization.

SHAW, Chattanooga, Tenn.

UNIVERSAL CALCINOSIS IN AN INFANT. B. SANCHEZ SANTIAGO and RAUL PEREIRAS, Arch. de med. inf. **9**:1 (Jan.-March) 1942.

Roentgenograms are shown of a 14 month old child in whom symptoms of calcinosis began at 5 months. These were localized edema and swellings of the extremities. Later plaques developed, which biopsy and roentgenograms showed to be calcium.

SANFORD, Chicago [AM. J. DIS. CHILD.].

A WEBER SYNDROME OF SYPHILITIC ORIGIN. ADHERBAL TOLOSA and V. VENTURI, Rev. neurol. e psiquiat. de São Paulo **5**:1, 1939.

This report concerns a case of syphilis in which the neurologic disorder evolved in three phases: (1) almost complete paralysis of the left oculomotor nerve; (2) appearance of right hemiplegia, predominating in the arm, face and tongue, a month later, and (3) slight involvement of the right oculomotor nerve. The symptoms appeared during active therapy with an arsenical compound, and the hemiparesis developed as a reaction to the inauguration of malarial therapy. The signs disappeared gradually with continued treatment, only slight paresis of the oculomotor nerve persisting. The authors explain the patient's difficulties on the basis of a spreading basilar meningitis of syphilitic origin in the peduncular region.

• BAILEY, Chicago. [ARCH. NEUROL. & PSYCHIAT.]

PARATRAUMATIC (PYOGENIC) ECZEMA. N. L. ROSSIANSKY, Sovet med., 1942, no. 10, p. 12.

The author states that around some wounds there may appear an inflammatory condition of the skin which clinically resembles eczema. This dermatosis appears around infected and slow-healing wounds, and it has occurred in spite of early aseptic and antiseptic surgical intervention, although not often. The dermatitis starts with elements similar to those of impetigo and folliculitis. As the disease progresses, the eruption becomes diffuse. The skin is red with a bluish tinge, edematous and infiltrated and is covered with yellow-greenish crusts. The borders are abrupt and round. There is some degree of itching and weeping.

A study of 83 cases revealed the presence of the following organisms: in all cases, Staphylococcus albus; in 60 cases, Staphylococcus pyogenes aureus and Staphylococcus albus, and in 24 cases Staphylococcus pyogenes aureus, Staphylococcus albus and hemolytic streptococci.

The author recommends the following treatment: In the weeping stage dressings wet with 6 per cent solution of aluminum acetate (Burow's solution) or 0.5 per cent solution of silver nitrate or gentian violet (methylrosaniline) diluted 1:1,000. As soon as the weeping and acute stages subside, he recommends the use of sulfur and tar ointments, starting with 2 per cent tar and 4 per cent sulfur in paste of zinc oxide (Lassar's paste) and increasing gradually to 5 per cent tar and 10 per cent sulfur. For in chronic and non-responding eruptions roentgenotherapy is suggested. There is no shortage of sulfonamide compounds in the Russian army; however, the author does not mention their use in this series of cases.

GRADOW, San Francisco.

NOSCOMIAL TRANSMISSION OF ECZEMA VACCINATION. ROLF BERGMAN and JONAS LINDAHL, Nord. med. (Hygiea) **11**:2714 (Sept. 20) 1941.

A 6 month old boy with eczema was admitted to a ward where 3 other infants with eczema and the healthy infants of 2 wetnurses were lying. All of the children were unvaccinated. After two days the boy's eczema showed a vaccine-like character (positive corneal reaction). His sister at home had been vaccinated three weeks previously. The boy was immediately transferred to an isolation hospital. The other 3 eczematous infants were also infected with vaccine virus, and so was also another infant with eczema from an adjacent ward. All 5 infants of the ward recovered, with remaining scars.

WALLGREN, Göteborg, Sweden. [AM. J. DIS. CHILD.]

Society Transactions

NEW YORK DERMATOLOGICAL SOCIETY

RAY H. RULISON, M.D., *Chairman*

A. BENSON CANNON, M.D., *Secretary*

March 23, 1943

Pigmented Lesion of Cheek. Presented by DR. EUGENE F. TRAUB.

T. Z., a child aged 2½ years, has twice previously been presented.

DISCUSSION

DR. A. BENSON CANNON: I think one should regard the pigmented lesions in the scar as being part of the original growth. I should never consider the patient cured until there has been a lapse of twenty to twenty-five years, as melanoma has been reported to have occurred as long as twenty-five years after removal of the original tumor. I believe that at the previous meeting of this society Dr. Kingsbury presented a patient in whom the melanoma had appeared at the site of the removal of a pigmented mole eight years previously.

DR. GEORGE M. LEWIS: Time alone will tell, but one point in favor of the lesion's being benign is the fact that no new lesions have developed in the period of observation.

DR. GEORGE M. MACKEE: The question can be settled by biopsy. I suspect the dark, pinhead-sized lesions to be blood vessels—or so-called blood cysts. Of course there is a possibility that metastasis occurred before the operation, but I am inclined to be optimistic.

DR. FRED WISE: I vividly recall the original lesion in this patient's cheek. There was much more visible pigment at the first and second demonstrations, and the appearance now is remarkably improved. The results are excellent, and I am much pleased with the present appearance of the cheek.

DR. GEORGE C. ANDREWS: Like Dr. Wise and Dr. MacKee, I am optimistic. The appearance is greatly improved. It is a well established fact that melanoma in infants and children is less malignant than in adults, and we would not necessarily expect a rapid extension of disease. I think the child must be kept under observation, and in the course of time it may be desirable to perform a biopsy of some of the brown spots on the face and remove a lymph node from the posterior cervical region, which will probably aid the diagnosis more than examinations of the lesions on the face. In the series of cases reported by Dr. Adair and Dr. Pack, of Memorial Hospital, they found that the subungual type of melanoma and melanomas in infants and children are less malignant than those in adults.

DR. EUGENE F. TRAUB: The point made about a melanoma's being less malignant in infancy is based, I imagine, not on the fact that the patient is an infant but on the fact that the melanoma arose from a pigmented nevus that had been present from birth. It is known that a malignant melanoma arising from such a lesion has a much better prognosis, even when it metastasizes, than does a melanoma that has arisen from a pigmented mark present only for a short time. Thus, a pigmented lesion that develops in an adult and has been present for only a few months or years is apt to give rise to a more malignant melanoma. In the case of this patient, it is the fact that the pigmented lesion was present at birth that makes me feel particularly encouraged about the outlook. Nor am I so much concerned about the peculiar stellate pigmented marks that have arisen in the skin graft as I am about the chain of palpable nodes present on the side of the lesion. These, of course, may be purely inflammatory. Recently the child has had peculiar pains in his feet which sometimes causes him to wake up in the night crying. The family physician considers the possibility of internal metastasis as a cause for this. However, a year and a half has passed since the original operation and apparently nothing has developed. Dr. MacKee's interpretation of the peculiar stellate pigmentation on the face as possibly blood pigment may indeed be correct, as it certainly does not look to me like a metastatic melanoma.

Angiokeratoma. Presented by DR. JOHN C. GRAHAM.

M. C., a woman aged 38, presents a keratotic area studded with dark brown masses on the plantar surface of the fourth toe on the right foot. The thickening of the skin and discoloration have been present for five or six years, but the patient paid no attention to this until April 19, 1941, at which time she had pain in this toe, which felt as though a hot wire were boring into it. The patient has never frozen her feet or had chilblains. She consulted a physician, who began to remove the rough skin, and since that time, on his instructions, she has frequently soaked her feet and removed as much of the keratotic area as possible.

On the fourth toe of the right foot is seen a sharply outlined plaque which is violaceous. There is some telangiectasia, together with several brownish, adherent, pinhead-sized plugs which are covered by a thickened, smooth and translucent epidermis. This area extends from the base of the toe to the distal end on the plantar surface.

Histologic examination showed the epidermis and traces of the corium in the papillae between the rete pegs. There was a thick layer of hyperkeratotic and parakeratotic material on the surface of the epidermis in a wavy, lamellar arrangement. The stratum granulosum was thickened in some areas, and some of the rete pegs were elongated. There were several spaces or sacs in the epidermis and in the papillae which were filled with blood. There were several dilated capillary blood vessels in the apexes of the papillae. There was no cellular exudate in the corium. The histologic diagnosis was angiokeratoma.

DISCUSSION

DR. EUGENE F. TRAUB: This is a peculiar-appearing lesion. The epidermis is white and looks almost as if phenol has been applied, and in the center it seems almost as if the epidermis has separated and a blister has formed. I believe boric acid ointment and an occlusive dressing should be applied to the lesion before final judgment is made, but if it is as reported histologically, an angioma with keratosis, it should be recorded as an angiokeratotic lesion rather than a true angiokeratoma.

Verruca Plana (Resistant to Treatment). Presented by DR. GEORGE M. LEWIS.

F. L., a woman aged 28, is presented from the New York Hospital. She had an ordinary wart on the right middle finger for fifteen years. One and a half years

ago small flat warts began to appear on the face, and this has continued to date. She consulted five different physicians, all of whom treated her for acne vulgaris. A sixth physician, a dermatologist, recognized the disease as verruca plana. Previous therapy has consisted of: (1) ten roentgen treatments (for acne); (2) one treatment by electrodesiccation to two or three lesions; (3) one treatment by electrolysis; (4) two applications of trichloroacetic acid; (5) twelve injections of sodium cacodylate; (6) ten injections of bismuth subsalicylate in oil; (7) twelve injections of antimony and potassium tartrate; (8) two courses of mercury protiodide (¼ grain [0.015 Gm.] daily for two weeks and ¾ grain [0.045 Gm.] daily for three weeks); (9) application of a peeling lotion; (10) six ultraviolet irradiations, and (11) removal of the common wart on her finger.

On examination there are numerous flat skin-colored verrucae on the face. A few lesions are present on the fingers.

DISCUSSION

Dr. A. Benson Cannon: In a number of cases I have seen spectacular cures follow the use of wart vaccine. Sometimes the warts will disappear after the first two or three injections, while in other cases eight to twelve treatments are required. I have used wart vaccine for a good many years, and my observation has been that approximately 60 per cent of warts are cured by its use. I have also had spectacular cures of warts involving the entire face, so closely studded as not to leave room for the head of a pin between them. I curet the warts, apply 50 per cent phenol and neutralize it with 70 per cent alcohol. I have an assistant spray the skin with ethyl chloride and with quick strokes go all over the face with a curet, the entire operation requiring only two to five minutes. Hot applications of solution of boric acid are then made, followed by a calamine lotion containing boric acid. The patient looks little the worse after completion of the work. Fully 70 to 80 per cent of the warts are cured with the first treatment, the remaining ones usually being removed at the second visit; few require a third. I have cured warts by this means when all other methods tried by a number of specialists have failed. The complexion is greatly improved by this method, and no scars result.

Dr. George M. MacKee: In the first place, this is not a severe eruption from the standpoint of number of lesions—just a stubborn one. Secondly, the patient has had a number of kinds of treatment, but there are some she has not had. Sometimes spectacular results are achieved in a case of this type with one intramuscular injection of sulfarsphenamine. Dr. Cannon mentioned vaccine. Dr. Biberstein, at the New York Skin and Cancer Hospital, has been getting about 70 per cent good results with wart vaccine. Incidentally, the substance is not a vaccine but a suspension of wart tissue. Curettage alone is sometimes successful. Sometimes the lesions require curettage followed by an application of trichloroacetic acid or phenol.

Dr. Howard Fox: There is no doubt in my mind about the efficacy of mental suggestion in causing the disappearance of both common and flat warts in children and adolescents. I have often felt that the effect of administration of mercury protiodide may be due to suggestion. In obstinate cases I should not hesitate to remove flat warts with a sharp bone curet, but I am opposed to the use of electrodesiccation, which is too apt to leave scarring.

Dr. Fred Wise: I have had the same experience as Dr. MacKee—obstinate eruptions which have not responded to ordinary methods have been cured by one injection of sulfarsphenamine. Biberstein, at the New York Skin and Cancer Hospital, recently demonstrated cases in which the lesions were treated with a wart emulsion, with complete cures; I believe this to be the ideal treatment, free of danger or after-effects. The emulsion is prepared by Dr. Biberstein.

Dr. Eugene F. Traub: For many years I have used so-called wart vaccine on all types of warts. I have used the preparation frequently as an autogenous vaccine and have obtained the best results in cases of flat warts. Other types of warts occasionally respond but not so frequently.

Dr. George C. Andrews: In connection with this case, I agree about the treatment but I am of the opinion that ultraviolet irradiation favors the growth of flat warts. The worst involvements I have seen have been in persons who owned ultraviolet lamps. This woman had ultraviolet irradiation, and I believe it was definitely wrong. What is really remarkable is the rapidity with which such flat warts will disappear, sometimes over night. I recall a case in which I gave arsphenamine, not sulfarsphenamine; the patient was covered with warts. I gave the drug for three days in succession, and when I saw him two days later they were all gone. It is hard to believe that such a transition can occur so rapidly.

Dr. George M. MacKee: It is a well known fact that it is often possible to cure warts by psychotherapy. That brings up the question of the mechanism of cure with so-called vaccine. One might think its effect was purely psychic, but it happens that the best results are obtained in cattle. Cows have warts which are large and numerous, and the vaccine appears to be almost a certain cure for them. One hesitates to credit psychotherapy for the result in cows.

Dr. Ray H. Rulison: When I first practiced dermatology I was associated with the late Dr. Whitehouse. A patient was seen with flat warts on his face, and Dr. Whitehouse got out his curet, scraped off the warts, put down the number on the chart, adding it to the number of those removed previously. The total was in the nine hundreds. I asked him how long he had been treating the patient, and he said seven or eight years.

Ochronosis. Presented by Dr. A. Benson Cannon.

M. L., a white woman aged 79, was admitted to City Hospital, Welfare Island, on Dec. 29, 1942, complaining of severe pain in the region of the left kidney and the left leg of three years' duration, with an acute exacerbation during the past three weeks. The past history was irrelevant except for "rheumatism" seven years previously and a burn on the buttocks fifteen years previously. There was no history of ingestion of drugs or phenol.

Examination shows brownish blue deposits in the cartilages of both ears, seen best with transillumination. The scleras show a slight diffuse dark bluish pigmentation. The scar of a burn is present on the right buttock. General physical examination discloses arteriosclerotic heart disease with hypertension.

Roentgenograms revealed osteoarthritis of both hip joints, both shoulders and the thoracic portion of the spine, with thinning and calcification of the intervertebral disks. Calcification in the cartilages of both ears and in the front parts of the shoulders was demonstrated by roentgen rays. Osteoporosis of the bones of both hands and feet was also shown.

Chemical examination of the blood showed normal values for sugar, nonprotein nitrogen, phosphatase, uric

...and total ester cholesterol. The complete blood ...ent was normal except for moderate secondary ...emia. Examinations of the urine have consistently ...own melanin and homogentisic acid. The latter has ...en gradually disappearing in the last month.

The patient's daughter has both melanin and homogentisic acid in the urine, without any signs or symptoms of disease.

DISCUSSION

DR. FRED WISE: I believe this is the first case of this kind presented before this society.

DR. A. BENSON CANNON: I presented a patient with much more extensive ochronosis before the Section of Dermatology and Syphilis of the New York Academy of Medicine about ten years ago. That patient was from my service at the City Hospital. Unfortunately roentgenograms of her bones were not made; it was not known at that time that ochronosis affects the osseous system, and it was thought that the deposits of pigment were confined to the cartilaginous tissue.

DR. NATHAN PENSKY (by invitation): One especially important observation is fusion of the bodies of the vertebrae in association with loss of definition of the borders, so that one could not see the delineation of the bodies. That was an important feature to the roentgenologist. There were also osteoarthritis of the joints and osteoporosis. The characteristic features of this disease are found in the syndrome rather than in any one aspect. There was not actual fusion of the bodies of the vertebrae but close approximation, with loss of delineation between them, the fault lying in the intervertebral disks. The roentgenologist made a diagnosis of ochronosis from those features. He stated that they were produced by pressure from the pigment.

Tinea Capitis (Trichophyton Violaceum). Presented by DR. GEORGE M. LEWIS.

J. A., a boy aged 11, is presented from the New York Hospital. For the past eight years a fungous infection has been present on the scalp. The infected hairs are broken off close to the scalp, resulting in the so-called black dot appearance. Trichophyton violaceum has been cultured. There are also erythematous scaly lesions on the back of the neck and face. He was presented before the Manhattan Dermatologic Society in October 1941. Therapy has consisted in epilation with roentgen rays and use of various local remedies.

DISCUSSION

DR. GEORGE M. MACKEE: At the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital tinea capitis caused by Microsporon audouini has been successfully treated with a fungicidal agent (benzoic and salicylic acids) in a liquid vehicle that penetrates keratin. It infiltrates the horny layer and the hair and extends down the follicle to the hair bulb. Thus far all infections have been cured in about three months. The vehicle is composed of a combination of wetting agents, glycols and synthetic alcohols.

DR. HOWARD FOX: My experience with "black dot" ringworm is limited. I tried epilation by means of roentgen rays in 1 case for the second and third times. The epilation was successful, but the disease was not helped. Although the hair eventually returned completely, its return after the third epilation was extremely slow; this experience made me resolve never to give more than one epilation to the scalp. Although infection with T. violaceum seems resistant to treatment, at least it does not appear to be as contagious as certain other species. This patient's brothers and sisters have not contracted ringworm.

DR. FRED WISE: I have had only one personal experience with an infection of this kind; the patient was a young boy for whom the usual local remedies proved to be futile. I transferred the patient to a physician who treated the ringworm with cataphoresis with copper sulfate; the patient was cured after three months of such treatment applied once a week.

DR. A. BENSON CANNON: I have successfully cured 3 patients with tinea capitis (Tricophyton violaceum) with the use of manual epilation followed by painting the lesions with 50 per cent phenol and neutralizing with alcohol as soon as the scalp became white. I had the patients use antiseptic applications at home either of gentian violet (methylrosaniline) or an ointment containing salicylic acid and sulfur. The cure required from two to three months. The late Dr. Kyrle, of Vienna, used to teach (in 1925) that any ringworm of the scalp could be cured by converting the infection into the kerion type by the application of tincture of cantharides. I am convinced that the cure results from the manual epilation plus the inflammatory reaction produced by the phenol or cantharides and not by antisepsis.

DR. GEORGE M. LEWIS: There is a possibility that occasionally patients with this infection experience a spontaneous cure. I recall 1 patient apparently cured while receiving indifferent therapy. This child has been given iontophoresis, roentgen epilation and many other procedures and treatments, without more than temporary effect.

Perifolliculitis Capitis Abscedens et Suffodiens. Presented by DR. A. BENSON CANNON.

B. G., a Negro truck driver aged 26, was admitted to City Hospital on Oct. 1, 1942 because of "boils" on the head of eight months' duration. About ten months prior to his admission he had used a patent hair straightener known as "Teek." Within a week boils appeared on his scalp; these were painful and spread from the occiput forward to the frontal area. In about two months the disease spread to the armpits and groins. As time went on, the lesions ruptured spontaneously and emitted pus constantly. The size of the lesions on the scalp and the pain became progressively greater until he was forced to give up work. He was treated at another hospital for about eight months with local wet dressings, which gave little relief.

On his admission to City Hospital, there were seen throughout the entire scalp soft fluctuant pea-sized to walnut-sized tender masses exuding thick greenish yellow pus. On compression of one lesion, pus exuded from neighboring masses, and irrigation through any one would produce pus from four or five different lesions. It was obvious that there were tunneling and dissection of the sinuses. The same process, though to a lesser extent, was seen in the axillas and groins with extension toward the pudendal areas. From the day of admission he had an intermittent type of fever, with the temperature at times as high as 103 F.

The total white blood cell count was 14,000 on admission, with a predominance of polymorphonuclear cells. The Wassermann reaction of the blood was negative, and urinalyses gave normal results.

The report of a roentgen examination of the stomach and duodenum revealed a duodenal ulcer. Pus evacuated from the lesions on the head produced growths of both staphylococci and hemolytic streptococci.

For two weeks the patient was given sulfathiazole by mouth and local sprays with irrigations. His temperature remained elevated, and the lesions, which were now painful and nodular, showed no signs of regression. On October 15, with the patient under general anesthesia, longitudinal incisions were made through the masses of confluent nodules to improve drainage. Two days after this the temperature dropped to normal and remained so, but regression of the abscesses was rather slow. Daily instillation of sulfathiazole after irrigation with hydrogen peroxide effected some improvement. Sulfadiazine was substituted for sulfathiazole, with no apparent difference in effect. In the first week of January the treatment was changed to shampoos with soap and water followed by application of compresses of mercury bichloride, salicylic acid and alcohol and applications of saline solution and sodium bicarbonate. The nodules were first aspirated, and then 5 per cent phenol was instilled. This treatment was given daily, and milk was injected intramuscularly twice weekly, producing chills with elevations of temperature to 105 F. An epilating dose of unfiltered roentgen rays was administered to the scalp, axillas and groins. In the scalp and axillas the condition is much improved. In the groins, pudendal area and perirectal region the disease is still active.

On Feb. 6, 1943, the patient grew tired of treatment and insisted that he be permitted to leave the hospital for a period of rest. He returns today for further therapy.

DISCUSSION

DR. GEORGE M. MACKEE: I agree with the diagnosis. The results are thus far excellent.

DR. FRED WISE: I agree with the diagnosis.

DR. EUGENE F. TRAUB: I presented a man before this society several years ago who had had the disease for over twenty years, with the eruption confined to the axillas and groin. Dr. Frank L. Meleney performed a wide surgical extirpation of the fatty tissue in all areas, with a dissection of the nodes, and packed the wound with zinc peroxide paste. For the first time the patient was entirely cured, despite the fact that previous surgical intervention of a more or less radical character had been unsuccessful. It is possible that Dr. Cannon's patient may be cured by a less radical operation, although I doubt it.

R. H. RULISON, M.D., *President*

A. BENSON CANNON, M.D., *Secretary*

April 27, 1943

Angioma Cavernosum with Fibrosis. Presented by DR. GEORGE M. LEWIS.

L. M., a baby aged 9 months, acquired a small lump on the chin following a bruise. This gradually increased in size until now it involves an area almost the size of the chin. The surface is reddened, with a blue tone in the peripheral part of the swelling. Unusual features are, first, a firm, almost cartilaginous base, and, second, pain when the lesion is manipulated.

A biopsy report from Dr. Foot stated that the lesion is "a vascular tumor in which the channels are firm plexuses just beneath the skin and in which there is almost as much cellular growth between the channels as there is in them. It is a plexiform hemangioma."

DISCUSSION

DR. EUGENE F. TRAUB: I am not exactly certain what the histopathologist means when he refers to this lesion as a "plexiform hemangioma." Examination of the slide shows the areas in which there are increased numbers of blood vessels, some of considerable size. However, many of the changes that are present are not to be found in any ordinary hemangioma, and there is a certain invasive character which suggests to me an infiltrating type of tumor. I believe it would be desirable to get further opinions on the histologic changes, as the lesion is certainly an unusual one.

DR. HOWARD FOX: I had the opportunity of seeing this patient in Dr. Traub's office. At that time I thought the lesion was an angiofibroma or angiosarcoma. It was hard and apparently had a fibrous or sarcomatous element.

DR. GEORGE M. LEWIS: There is considerable fibrosis but no evidence of sarcomatous change. The question in therapy is whether radium or refrigeration therapy would be of any benefit because of the fibrosis.

DR. EUGENE F. TRAUB: I should be against any type of refrigeration for this lesion. Regardless of whether on the basis of a microscopic examination the cells appear to be radioresistant or radiosensitive, I suggest giving at least one rather intensive dose of radium to see what response occurs. If a favorable response takes place, then the advisability of further radium treatments could be considered. If no response occurs from the irradiation, then surgical intervention is indicated, and certainly the single dose of radium would not handicap any subsequent surgical measures.

DR. FRED WISE: I agree with Dr. TRAUB's therapeutic suggestion.

A Case for Diagnosis (Lupus Erythematosus? Lichenoid Sarcoid?). Presented by DR. FRED WISE.

Mrs. S. D. S., aged 41, was referred to me by Dr. H. G. Miskjian, of Cleveland, who presented her before the Cleveland Dermatological Society as having lupus erythematosus of the face and lesions on the back and outer aspects of the arms. The latter consist of groups of perifollicular macules and isolated colorless infiltrated nodules. The duration of the eruption is approximately one year.

Physical examination by her physicians in Cleveland showed no gross abnormalities. The patient complains of occasional pains in various joints and attacks of low grade fever, the temperature ranging from 99 F. in the morning to 100.4 F. in the evening, most often preceding the menses.

In November 1942, Dr. Machacek examined a piece of tissue removed from an infiltrated nodule in the midarea of the back, but he stated that the histologic changes were too meager and ill defined to enable him to offer a diagnosis.

The eruption is located on the nose, cheeks, neck and scalp, and on the upper portion of the back and outer aspects of the arms. The lesions on the scalp, face and neck appear to be lupus erythematosus which has become more or less crusted and hyperkeratotic, so that the typical surface markings of the eruption have been partly obliterated. The lesion situated under the chin was preceded by an infiltrated nodule.

The eruption on the back and arms is composed of two different forms of lesions. One is a widespread reddish yellow eruption of pinhead-sized, grouped perifollicular macules, some of which are slightly depressed and form stippled scars, which appear to be situated in the follicular orifices. The other consists of pea-sized to dime-sized scattered infiltrations which are well defined and firm to the touch, their color varying from

shade of normal skin to pink and light red. These are irregularly scattered over the back and outer surfaces of the arms and appear to form a part of the perifollicular eruption.

On the crown of the head are several dime-sized areas of total alopecia with obliteration of the hair follicles and beginning atrophy of the scalp.

The diagnosis of lupus erythematosus of the face and scalp and lichenoid sarcoid of the back has been entertained by several expert dermatologists. The nodular infiltrations were regarded as possibly being the early stage of anetoderma.

A section for histologic study was removed from an infiltrated lesion on the back on the day preceding this presentation.

NOTE.—The section showed nothing more than a mild urticarial reaction.

DISCUSSION

DR. HOWARD FOX: I think that this is a single dermatosis, lupus erythematosus, and also that lupus erythematosus is one of the greatest imitators of other diseases of the skin, both clinically and histologically.

DR. A. BENSON CANNON: I think that tuberculosis would explain the patient's varied lesions as well as her symptoms of fever, malaise and glandular enlargement.

Pityriasis Rubra Pilaris. Presented by DR. HOWARD FOX.

Miss J. E., aged 45, a travel agent born in Scotland, suffered from a similar eruption in 1908. At that time, she was a patient of Dr. George H. Fox in his service at the New York Skin and Cancer Hospital. A positive diagnosis was made of pityriasis rubra pilaris, which eventually became a universal exfoliating dermatitis with temporary loss of hair and eyebrows. She was under observation as a bed patient for six months and as a dispensary patient for the following five years. At the end of this period the eruption had entirely disappeared. She then went to Milwaukee, where she remained until 1926. She returned to New York and remained well for thirty years following her first attack.

The present eruption appeared about two months ago as diffuse patches on the scalp, face and neck which resembled seborrheic dermatitis. It has recently changed in appearance and has become generalized, symmetric and profuse. There are areas of redness with fine scaling and well defined borders. On the edges of some of the areas are pinhead-sized acuminate papules, and between areas of the eruption are irregularly shaped islands of normal skin. There is considerable hyperkeratosis of the palms. The hair is becoming thin and shows a profuse amount of fine white scales.

The patient is well nourished and in fair general health. She gives no history of night blindness. She is being treated with vitamin A, 200,000 U. S. P. units daily by mouth.

DISCUSSION

DR. FRED WISE: I agree with the diagnosis of pityriasis rubra pilaris.

DR. FRANK C. COMBES: I agree with the diagnosis, but I think that one occasionally sees islands of normal skin such as this patient shows in some patients with psoriasis. This patient does not show the typical acuminate and obtuse papules characteristic of this disease, but I do not doubt that they have been present at some time and have been observed by Dr. Fox, who has attended her for many years. I was interested to hear that in some patients the skin is completely covered. In every patient I have seen there has always been one or two small islands of normal skin.

DR. HOWARD FOX: It is a well known fact that pityriasis rubra pilaris is one of the half-dozen diseases which may become universal; that is, it may involve every inch of the cutaneous surface. That was the condition of this woman when she was in my father's service at the New York Skin and Cancer Hospital. She was in the hospital for six months, and all members of the staff had a chance to study her case. An unquestioned diagnosis was made. Some one remarked about the long remission as being unusual. In the famous case of Bertha Schmidt, whose photograph appears in my father's Atlas, there was a complete remission for fourteen years while she was living at the seashore.

A Case for Diagnosis (Lupus Erythematosus?). Presented by DR. GEORGE M. LEWIS.

M. O., a nurse aged 22, is presented from the New York Hospital. In November 1941, a chalazion was removed from the right lower eyelid. The operation was repeated for a similar condition in August 1942. Redness of the right lower eyelid, with progressive involvement of the lid accompanied by loss of cilia, has been noted for the past year and a half.

On examination, the margin of the lower lid on its outer third shows a bright red slightly elevated lesion. When the lid is everted, the same condition is also seen on the inner surface. No atrophy has been noted. A linear scar at the site of operation is present.

The histologic examination by Dr. Foot showed a mass of connective tissue covered by epidermis and studded with islands of lymphoid cells which seemed to have little anatomic relation to any of the elements of the skin. They did not show definite perivenous localization and were seen about hair follicles rather more frequently than elsewhere. The lesion was more suggestive of chronic folliculitis than it was of anything else.

DISCUSSION

DR. FRANK C. COMBES: I agree that the diagnosis as presented is the most likely. Since this is a small lesion, one might try intradermal injection of a gold salt.

DR. A. BENSON CANNON: I suspect that the patient has a keloidal scar as a result of the removal of the chalazion. I should think that irradiation plus cauterization would suffice to flatten the scar.

DR. GEORGE M. LEWIS: There has been progressive increase in the size of the patch of redness of the lid and progressive loss of cilia for one and a half years. The obtaining of the specimen for biopsy removed a good part of the lesion, but there is still much active disease. The histologic picture does not help the diagnosis of lupus erythematosus.

Erythema ab Igni. Presented by DR. EUGENE F. TRAUB.

E. Van A., a man aged 33, has worked since Aug. 24, 1942, for the Columbia Aircraft Company as an inspector of aircraft. He contacts all kinds of metals—steel, aluminum (duralumin) and others. On Feb. 27, 1943, he felt what appeared to be a sty on the left eye and applied solution of boric acid to it. A few days later it began to inflame the upper and lower eyelids.

The nurse at the plant referred him to a physician, from whom he received treatment. As the eye did not improve, on March 3 he consulted his family physician. He in turn referred the patient to an ophthalmologist. The patient remained at home from March 5 to March 30 under his care and under the care of his wife, who is a nurse. Compresses of hot solution of boric acid were applied, and he took sulfadiazine tablets. The eruption improved, but since a slight eruption remained, the patient was referred to me for diagnosis and opinion.

Examination shows a solid area of erythematous pigmentation involving the outer two thirds of the upper lid and extending around onto the lower lid of the left eye, where the pigment has assumed a reticulated appearance with little erythema.

DISCUSSION

DR. FRANK C. COMBES: I agree with the diagnosis of erythema and pigmentation from the application of heat. However, I was under the impression that the pigmentation in erythema ab igni is more or less permanent. If this is so, is the term applicable to this lesion, which is disappearing?

DR. HOWARD FOX: I agree with Dr. Combes that at present this is merely pigmentation, which could be called chloasma. Pigmentation can be caused by heat, cold, ultraviolet irradiation, roentgen rays and all kinds of physical agents locally applied.

DR. GEORGE M. LEWIS: I should like to ask if Dr. Traub has considered that the local use of eye drops may have been of etiologic significance.

DR. EUGENE F. TRAUB: If I recall correctly, the treatment consisted chiefly of hot solution of boric acid compresses and sulfadiazine tablets taken internally. If the patient used any eye drops I do not know anything about it. I believe in the beginning he did have one application of a silver preparation to the eye.

DR. MAURICE COSTELLO (by invitation): I agree with the diagnosis of Dr. Traub, that this patient has a localized erythema ab igni. I should like to ask him if the patient had used a small electric heating pad on this area. I have never seen a localized eruption of this nature from the use of sulfonamide compounds.

DR. EUGENE F. TRAUB: I am sure that if I had presented this patient as having chloasma, I would have been told that he had erythema ab igni due to the application of heat. There is no question about the correct diagnosis, and the degree of permanency is absolutely unimportant. Erythema ab igni depends for its permanency on repeated insults over a long period, and when this does not occur the process is not permanent.

Hyperpigmentation (Arsenic?). Presented by DR. R. H. RULISON.

A. R., a Negress aged 41, gives a history of pneumonia in 1940, an operation for removal of a fibroid tumor in 1938 and an injury to the right eye, with enucleation, in 1913. At the time of the operation for fibroid tumor, a routine Wassermann test showed a 4 plus reaction. No serologic examination had ever been performed prior to that time. No history of primary or secondary lesions can be elicited. On March 22, 1939 antisyphilitic therapy was instituted, and between then and April 22, 1942 she received, irregularly, twenty-two intravenous injections of mapharsen and seventeen intramuscular injections of bismuth subsalicylate in oil. Save for occasional nausea from the arsenical, the medications were well tolerated.

In April 1942 the patient presented herself with lesions of one month's duration. The eruption was generalized and consisted of "blotchy" areas of muddy gray-brown pigmentation with a suggestion of erythema. The latter feature was not clear on the normally darkly pigmented skin. The pigmented areas varied in size from that of a pinhead to that of a palm, were mainly on the trunk, were discrete and confluent and showed no tendency toward assuming any definite configuration. It was advised at that time that all arsenicals be omitted.

The arsenicals were omitted, and the patient received only bismuth compounds. About six months after the aforementioned observation, she began to notice "white" areas on the skin of the face and later on the extremities and trunk. On one occasion, overnight, she noted the appearance of a white streak in the hair and a corresponding white patch on the scalp.

On April 8, 1943, she presented herself again, after she had not been seen for a full year. In addition to the pigmented areas noted before, there are now present variably sized (from the size of a pinhead to almost that of a palm) discrete and confluent patches of depigmentation. The old pigmented areas are still present, and in the areas which now show depigmentation, the old pigmentation is still present, retaining its original color.

Microscopic examination of a section of skin removed from a pigmented area on the normally dark Negro skin revealed that the epidermis showed slight nevoid changes, as evidenced by slight increase in the thickness of the horny layer, by a loosely laminated nature, by regional increase in the prickle cell zone and by a slightly verrucous surface. The palisade layer stood out clearly as a result of an abundance of dark brown granules in the basal cells. In some places the granules were noted in the prickle cell zone, but this was not the rule. The blood vessels of the cutis were normal, as were the adnexae. In the papillary and upper subpapillary zones of the cutis were noted many brown staining granules, most of them lying free but some contained within melanophores. The pigment in the basal cell layer reacted with dioxyphenylalanine (dopa), that in the cutis did not. The pigment did not react to the Perles stain for iron.

DISCUSSION

DR. MAURICE COSTELLO (by invitation): On several occasions I have had Negro women patients presenting this piebald appearance caused by partial depigmentation and various degrees of hyperpigmentation which followed a dermatitis medicamentosa due to the arsenicals administered in the treatment of syphilis. Dr. Cannon reported on similar eruptions several years ago.

DR. FRED WISE: I should like to ask whether eruptions like this do not appear occasionally in patients who have had no medication whatever.

DR. A. BENSON CANNON: I have encountered several similar cases of leukoderma, as well as vitiligo, following arsphenamine therapy. The patient usually has a dermatitis, followed by leukoderma and vitiligo with other areas of increased pigmentation. I reported cases of vitiligo following arsphenamine dermatitis a few years ago. I suggest that the patient's blood, urine and skin be examined for arsenic and that she be given sodium or calcium thiosulfate, forced fluids and a suitable diet to eliminate the arsenic. Usually, most of the depigmented areas will eventually return to normal color.

DR. H. RULISON: What particularly interested me in this case was the deposit of pigment below the basal cell layer in the papillary body, which was not at all changed apparently by the later development of vitiligo involving all the pigment cells in the basal layer in the areas of vitiligo while the hyperpigmentation persisted in the corium. I thought that this was interesting. I should like the opinion of the members as to whether this is a common observation.

DR. HOWARD FOX: I do not think it is quite proper to speak of this eruption as vitiligoid. Certainly most of it does not show complete depigmentation. This woman has a dark skin, and most of the depigmentation is incomplete.

DR. R. H. RULISON: In those areas there was first hyperpigmentation, due to a deposit of melanin below the normal location. The areas were extensive. On top of this vitiligo developed, and the normal pigment disappeared in the basal cell layer, but the hyperpigmentation, which was in the cutis, remained.

Xanthoma Diabeticorum (Xanthoma Eruptivum). Presented by DR. JOHN C. GRAHAM.

G. S., a woman aged 52, has had lesions coming out in crops around the joints for the past year. During the intermissions the subjective sensations are nil, but when the lesions are increasing there is considerable itching.

The patient presents on the elbows and knees pale yellow waxy lesions, some having a surrounding brown area. The separate lesions are 1 to 2 mm. in diameter and slightly raised. On the back and thighs the patient also presents several patches of brown lesions, most of which are flat; in the center of each lesion is a black dot apparently involving the follicular opening. A few of the lesions have slight induration, but most of them are not palpable. They are irregularly shaped and brown.

The blood count was normal. The urinalysis showed a 4 plus reaction for sugar, and the examination of the blood for sugar showed 235 mg. per hundred cubic centimeters. The diagnosis of diabetes was made for the first time three weeks ago. Until this time the patient has had no treatment, and she is now only on a restricted diet and is not taking insulin. She was seen by members of the dermatologic department for the first time only a few days ago.

DISCUSSION

(The members were in unanimous agreement with the diagnosis as presented.)

Dermatitis Artefacta. Presented by DR. FRED WISE.

M. L., an unmarried woman aged 35, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on March 27, 1943, presenting lesions of twenty months' duration. Her father died at the age of 35 of tuberculosis of the lungs. Her mother has diabetes. One of her four sisters has tuberculosis of the lungs. The patient had measles, pneumonia and frequent colds as a child and typhus in 1920. She has been having "stomach trouble" since 1929. For the past three years she has been treated at the Kings County Hospital for "ulcerative colitis, kidney trouble and pyelitis." Two years ago she had a "streptococcic sore throat." During this time she had frequent attacks of pain, diarrhea and bloody stools. The patient states that she lost about 45 pounds (20 Kg.) during the past year. She has been vomiting once or twice daily for the past two months, the vomitus being sometimes bloody.

Lesions developed first on the anterior surface of the left thigh, "one sore developing after another." Those healed within a month, leaving scars. Similar lesions developed six months later in the corresponding area of the right thigh and later on the abdomen.

The patient looks sickly and pale. She complains of feeling weak. She steadfastly denies on repeated questioning that the lesions have been produced by herself, stating that "I would be crazy to do that."

The lesions are numerous and distributed in a symmetric fashion on the easily accessible parts of the body. They are located on the entire abdomen and on the dorsal surfaces and sides of the thighs, ending almost in a straight line at the upper surface of the knee joints. There are no lesions on the front of the chest except for a few at the nipple areas. The entire posterior surface of the body is free of lesions. Those on the left thigh are mostly circular and discrete and consist for the greater part of depressed white pea-sized to dime-sized scars with even floors. The lesions on the right thigh consist of a conglomeration of roughly circular and oval lesions. Many of these scars are white, while others are brownish pigmented. The lesions on the abdomen are more closely grouped and consist mostly of oval pigmented patches and scars, roughly of about the same size. There are several active deeply punched-out ulcerated areas. There are also several plum-sized to egg-sized raised painful and ulcerated abscesses distributed on the abdomen.

The nasopharyngeal reflex is diminished. The conjunctival reflexes appear normal. Results of routine laboratory tests were normal, except for the hemogram, which showed a moderate anemia.

DISCUSSION

DR. HOWARD FOX: This is a classic picture of an eruption in a drug addict who uses an unsterile syringe and injects a narcotic drug into accessible areas. I am certain that this patient uses a narcotic. She gives a history of having had a great deal of pain and may have used drugs for that purpose. The mere fact that she is unwilling to admit the use of a narcotic drug does not invalidate the diagnosis. Most of the patients I have seen with an eruption of this type have been men. I should call this eruption dermatitis traumatica rather than dermatitis factitia.

DR. EUGENE F. TRAUB: I agree with Dr. Fox that nothing but a hypodermic injection can produce lesions like these and the ones which show erythematous nodules or tumors present today.

DR. FRED WISE: This is the first case I have encountered in which I have not been able to get any admission from the patient that he has been taking a narcotic by means of the hypodermic needle.

A Case for Diagnosis (Erythema Multiforme?). Presented by DR. GEORGE M. LEWIS.

S. G., a war correspondent aged 31, was previously presented, on April 13, 1943, at the Manhattan Dermatologic Society.

At the present time there are semicircular erythematous scaly and crusted lesions on the back of the neck. A few small pustules are also present.

Since the first presentation, a biopsy has been performed. The histologic slides were examined by Dr. Wilbert Sachs, who found no evidence of contact dermatitis. The epidermis showed intercellular edema. The outstanding feature was dilatation and congestion

of the vessels in the upper part of the cutis. It was his impression that the disease is toxic dermatitis.

DISCUSSION

DR. EUGENE F. TRAUB: Despite the fact that the first section did not suggest it, I believe this is typical benign familial bullous dermatosis (Hailey-Hailey). I have had 1 or 2 cases in which several biopsies had to be made before characteristic changes were found. I think a better term is benign bullous dermatosis which is sometimes familial.

DR. GEORGE C. ANDREWS: Do patients with Hailey-Hailey dermatosis have this redness?

DR. EUGENE F. TRAUB: They have redness exactly like that.

DR. A. BENSON CANNON: The lesion is characteristic of benign familial pemphigus as discussed by Hailey and Hailey. I feel, as Dr. Traub does, that a second biopsy should be performed.

DR. GEORGE M. LEWIS: The specimen taken two days ago certainly shows no evidence of dyskeratosis or any other classic features of Hailey-Hailey disease. It does show evidence of a toxic dermatitis such as one would find from a focus of infection or from the taking of a drug. However, no internal etiologic factor has been discovered.

Lupus Erythematosus Disseminatus. Presented by DR. FRED WISE.

C. F., an Irish woman aged 36, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 27, 1943, presenting lesions of three years' duration. She has pain on raising her arms.

On the face, lips, neck and ears is a scaly erythematous eruption. There is moderate edema of the face and eyelids. On the lower extremities is a scaly papular rash. The legs are painful on pressure. The ankles are edematous.

The Wassermann and Kahn reactions were negative. The hemogram revealed 3,950,000 erythrocytes and 4,100 leukocytes. The chemical examination of whole blood gave normal results for urea nitrogen, nonprotein nitrogen, uric acid, chlorides and dextrose. The ratio of urea nitrogen to nonprotein nitrogen was 46 per cent (normal, 35 to 45). Examination of the blood serum gave the following results: total proteins, 7.0 Gm. (normal 6 to 8); albumin, 3.1 Gm. (normal 4 to 5); globulin, 3.9 Gm. (normal 2 to 3); ratio of albumin to globulin 0.8:1 (normal 1.6 to 2.0:1). The sedimentation rate was 30 mm. per hour by the Westergren method (maximum normal for females, 15 mm.).

The physical examination gave normal results except for sonorous rales over the entire left side of the chest anteriorly and posteriorly. Examination of the eyegrounds for possible involvement revealed that in the perimacular region of the right fundus is a small area of exudative choroiditis and there is an area of choroidal exudate just inferior to the disk. These lesions appear to be recent.

NOTE.—The patient became acutely ill a few days after her presentation at this meeting. Shortly thereafter, she became maniacal and was removed to the psychiatric ward of Bellevue Hospital. I was unsuccessful in obtaining a section for histologic study.

Lupus Erythematosus, Extensive Discoid Type. Presented by DR. EUGENE F. TRAUB.

S. N., a man aged 29, visited the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 5, 1943, complaining of an eruption on his forehead, face, ears, neck, chest, back, arms, forearms, backs of the hands and soles, of four years' duration. The eruption first appeared on the butterfly area of the face during the summer. He consulted his family physician, who gave him some intravenous injections and instructed him to take sun baths. After a severe sunburn, the patient noticed that instead of the erythema's healing, bright red painful pruritic lesions appeared on his face, forehead, ears, neck, chest, back, arms and forearms. He was then referred to the Queens General Hospital, where the diagnosis of "lupus erythematosus" was made and he was advised to take injections of gold and bismuth preparations. For the next three months the patient received intravenous injections of a gold compound, given by a dermatologist, and this resulted in an improvement of his cutaneous lesions. Thereafter the patient consulted a chiropractor in an endeavor to get well more quickly and received chiropractic treatments to the spine for four months with no effect. He then consulted the family physician and for the past year he has received injections of a gold salt intravenously and of a bismuth preparation intramuscularly.

Two weeks ago new pruritic lesions began to appear on the dorsal surfaces of his hands and fingers. No history can be elicited that roentgen or ultraviolet irradiation has been administered.

During all this time the patient has been able to continue with his normal occupation as machinist, but he states that the eruption has been subject to acute erythema alternating with paling of the skin.

The past history includes pneumonia, mumps, measles and dental extractions two months ago (focus of infection). His family history was noncontributory. The physical examination revealed essentially normal conditions except for some firm nontender lymph nodes in the axillary and inguinal regions.

Examination of the eruption shows the following facts: On the forehead is a patchy erythematosquamous eruption. Some lesions appear papular and excoriated. Others, above the eyebrows, appear to be undergoing involution and are violaceous. The entire face and ears, the retroauricular area and the nape of the neck have the appearance of poikiloderma, or "x-ray skin," characterized by erythema and violaceous areas intermingled with pigmentation and white areas of fine scarring and atrophy. The whole eruption has a reticulated appearance and is essentially maculosquamous. The lips show a patchy, violaceous scaliness.

The entire middle portion of the front of the chest has a reticulated appearance characterized by erythema, pigmentation, adherent silvery scales and superficial scarring or atrophy. Similar isolated patches are present on the sides of the chest, over the shoulder blade areas and over the upper and middle portions of the back. Telangiectasia appears to be present in these regions.

On the outer aspects of the arms and forearms are grouped, diffuse regions showing erythema, adherent scales and superficial atrophy or scarring. On the dorsa of the hands and fingers are large, nummular acutely eczematous areas.

On March 31, 1943, biopsy of a lesion on the left arm showed lupus erythematosus. On April 10 biopsy of a lymph node in the left axilla was reported as follows: The section showed a large lymph node, the architecture of which was fairly well preserved. The lymph follicles were distinct, the sinuses narrow and the germinal centers moderately prominent. There was an irregular scattering of anthracotic pigment. Only in

ne are slight distortion due to hyperemia, edema and hemorrhage was noted. The peripheral sinuses in this area were dilated, and the sinuses and pulp cords contained a moderate number of plasma cells, some of them with two or three nuclei, large mononuclear cells and reticulum cells. The endothelial cells were moderately swollen. These changes, however, were limited to a small area. The diagnoses were: undiagnosed condition of axillary lymph nodes; anthrosis of lymph node. There was no histologic change that suggested lupus erythematosus.

The hemogram on April 6, 1943 showed 4,690,000 erythrocytes, 4.5 Gm. (87 per cent) of hemoglobin and 6,550 leukocytes, with 54 per cent polymorphonuclear leukocytes, 1 per cent eosinophils, 8 per cent monocytes and 37 per cent lymphocytes; there were 200,000 platelets. The bleeding time was four minutes and the coagulation time five minutes, clot retraction being completed in four hours. The prothrombin clotting time was normal (sixteen and one-half seconds). The Wassermann reaction was anticomplementary on numerous occasions. The Kahn precipitation test gave a negative reaction. Chemical examination of the blood showed 11.5 mg. of urea nitrogen, 31.5 mg. of nonprotein nitrogen (ratio of urea nitrogen to nonprotein nitrogen 36 per cent), 65 mg. of dextrose and 185 mg. of cholesterol per hundred cubic centimeters. The icteric index was 6.5, and the sedimentation rate was 32 mm. in one hour (normal 10 mm). The Hanger cephalin-cholesterol flocculation test gave a 3 plus reaction. The Addis count was essentially normal.

Determination of the vitamins gave the following results: vitamin A, 30 blue units (normal), and total carotenoids, 45 units per hundred cubic centimeters; vitamin C in the plasma, 0.5 mg. per hundred cubic centimeters (normal 0.7 to 1.4 mg.). The vitamin C saturation test gave a normal result.

The urine was normal. On April 7 examination of the urine for porphyrin showed excretion of 100 micrograms per twenty-four hours (normal 60 to 100). On April 10 guinea pigs were inoculated with material from half of the removed axillary lymph node. The result has not been reported as yet. On April 6 the electrocardiogram showed a deviation of the axis to the right and minor changes which might fit the diagnosis of lupus erythematosus. Dental roentgenograms on April 12 showed a few cavities. A roentgenogram of the chest on April 9 showed old puerile type central tubercle foci and scars with moderate secondary root branch and central bronchial thickening, mainly on the right. Tests with tuberculin in dilutions of 1 to 1,000,000, 1 to 100,000 and 1 to 10,000 produced negative reactions.

DISCUSSION

DR. MAURICE COSTELLO (by invitation): I believe this patient was presented primarily for suggestions as to therapy. I should like to suggest administration intramuscularly of 3 cc. of crude liver extract twice a week as the best form of therapy for this disease. It is harmless. The preparation contains 1 U. S. P. unit per cubic centimeter.

DR. GEORGE C. ANDREWS: Why use an extract containing 1 instead of 2 U. S. P. units of the liver per cubic centimeter? I had been using the material containing 1 unit per cubic centimeter and found that an extract is available that contains 2 units per cubic centimeter. The extract is originally made of that potency and is diluted down to 1 unit. Therefore, there is no advantage to using the 1 unit dose when a smaller amount can be used and 2 U. S. P. units per cubic centimeter given.

DR. GEORGE M. LEWIS: As a suggestion for therapy, Dr. Thomas Graham used autogenous and stock vaccinotherapy with good results.

A Case for Diagnosis (Parapsoriasis Varioliformis?). Presented by DR. FRED WISE.

J. C., an Italian man aged 63, registered at the Skin and Cancer Unit of the New York Post-Graduate Hospital and Medical School on April 24, 1943, presenting lesions of four weeks' duration. He states that he never had any eruption before and that he "was never sick."

A few papules appeared first on the flexor surfaces of the forearms. He applied tincture of iodine, which caused the forearms to swell. Similar lesions broke out a week later on the abdomen, and within three weeks the whole body became involved. There is only slight itching.

The patient is a robust-looking man. His general health seems to be unaffected. He has a generalized symmetric eruption involving the entire neck, trunk and limbs. The eruption is most pronounced on the arms, forearms, lower two thirds of the back, abdomen and thighs. All areas are affected on the upper and lower limbs, with a predilection for the volar surfaces. The lesions on the front and back of the chest follow more or less the distribution of the intercostal nerves. The hands are comparatively free of lesions.

The lesions consist of papules ranging in size from that of a pinpoint to that of the head of a match and somewhat larger. Some are umbilicated, revealing central pinpoint openings. Some are capped by fine scales, while others are covered with dried hemorrhagic crusts. The lesions are discrete, closely grouped and coalesced, the latter being predominant on the lower half of the back and abdomen, where they form irregular, bizarre purplish red raised patches covered with sparse adherent scales. These fade only partially on moderate diascopic pressure, revealing yellowish patches. Some of these patches, especially in the bathing trunk area and in the axillas, are devoid of epidermis, copiously bathed by somewhat mucilaginous yellowish fluid. There are a few tense bullae with firm and fairly thick walls containing clear yellowish fluid on the outer side of the left leg and on the posterior surface of the left heel. There are several linear lesions on the dorsal and flexor surfaces of the left wrist, which consist of coalesced flattened match head–sized papules resembling lichen planus.

The tongue is coated. There is a patch the size of a finger nail on the left buccal mucosa which consists of closely grouped pinpoint-sized to pinhead-sized whitish flattened papules intermingled with fine linear streaks.

The hemogram was normal except for 13 per cent polymorphonuclear eosinophils and 13 per cent band neutrophils. A cell count of fluid from an unruptured bulla showed normal values with the exception of 35 polymorphonuclear eosinophils.

A histologic section examined by Dr. Charles F. Sims was reported as "suggestive of parapsoriasis varioliformis." The description was as follows: There were a moderate and irregular acanthosis of the epidermis and slight hyperkeratosis and spotty parakeratosis, alternating with a retained granular layer. At several points there was an interstitial edema of the lower epidermis as well as a basal cell disorganization and a moderate exocytosis. The capillaries of the papillary bodies were decidedly dilated, and there was consider-

able edema of the collagen framework in the papillary and subpapillary zones. A moderate perivascular and diffuse cellular infiltration composed for the most part of small round cells was noted in the upper part of the corium. The blood vessels throughout the corium were moderately dilated and congested, and their walls were edematous.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

FRANK C. COMBES, M.D., *Chairman*
PAUL GROSS, M.D., *Secretary*
April 2, 1943

Mycosis Fungoides Simulating Parapsoriasis. Presented by DR. EUGENE T. BERNSTEIN and DR. LEWIS A. GOLDBERGER.

S. T., a man aged 65, is presented from Mount Sinai Hospital with erythroderma of the entire integument, except on the chest and the middle of the back, of ten years' duration. There have been no remissions.

The patient presents generalized rounded, partly discrete and partly sharply delineated scaly plaques of various colors, ranging from waxy yellow on the scalp, face and neck to brick red and bluish red on the extremities. On the outer aspect of the right thigh there is a horseshoe-shaped elevated and deeply infiltrated area about 4 inches (10 cm.) in diameter, the center of which is depressed, with a raised border 2 inches (5 cm.) wide. The infiltration is in a state of recession. The entire skin is dry and roughened, and many comedos are seen. Between the shoulders there are many long, sharp, spinous keratotic lesions ranging from 0.25 to 0.5 cm. in length.

When the patient was first observed, these lesions were three times longer than at present. The improvement is the result of a daily dose of 150,000 U. S. P. units of vitamin A for a total dose of 5,000,000 units.

The patient went to the New York Post-Graduate Medical School and Hospital in 1937, and a biopsy in October of that year suggested mycosis fungoides. As a result of another biopsy, two weeks later, the disease was diagnosed as perivasculitis. In 1940 a clinical diagnosis of parapsoriasis was made at the Morrisania Hospital, and in March 1941 a clinical diagnosis of parapsoriasis was also made at the Bronx Hospital. The patient came to the Mount Sinai Hospital on Oct. 20, 1942, at which time he showed general adenopathy, no pruritus and slight discomfort.

The Wassermann reaction of the blood was negative. The hemoglobin content was 60 per cent; there were 3,870,000 red blood cells and 11,200 white blood cells, with polymorphonuclear leukocytes 72 per cent, lymphocytes 16 per cent, monocytes 8 per cent and eosinophils 4 per cent.

Microscopic examination of tissue from the right thigh on October 21 showed a regular acanthosis of the epidermis, with elongation of the rete pegs and thin suprapapillary plates. There were some hyperkeratosis and some parakeratosis. The subepidermic region and the upper part of the cutis had a tremendous cellular infiltration and considerable edema, and the papillary bodies were elongated. Between the cellular elements was a fine reticulum. The cellular elements were small round cells, wandering connective tissue cells, a few plasma and epithelioid cells and considerable numbers of pyknotic cells. The microscopic diagnosis was "mycosis fungoides simulating psoriasis."

Mycosis Fungoides (Tumor Stage). Presented by DR. LEWIS A. GOLDBERGER and DR. EUGENE T. BERNSTEIN.

P. G., a woman aged 48, was previously presented before the Bronx Dermatological Society three months ago and before the New York Academy of Medicine twelve years ago. There are a generalized eruption of twenty years' duration with exacerbations and remissions and tumor formation of five years' standing.

DISCUSSION ON CASES OF MYCOSIS FUNGOIDES

DR. WILBERT SACHS: Dr. Chargin was always of the opinion that the woman had mycosis fungoides, though we were not able to prove it by microscopic examination. However, her disease did turn out to be mycosis fungoides. This is the only case I know of which was followed in this way, the disease being diagnosed as premycosis fungoides and later as mycosis fungoides. Possibly Dr. Chargin is correct in saying there is such an entity as premycosis fungoides, but just 1 case is not enough to justify a final statement. One should be a little more open minded until it can be proved more conclusively.

In the case of the man, there was nothing in the microscopic picture to suggest parapsoriasis. If one looks only at the epidermis, it is typical of psoriasis, not parapsoriasis. The disease was mycosis fungoides and not parapsoriasis.

DR. PAUL GROSS: I believe the statement of Dr. Bernstein about the specificity of vitamin A therapy for lichen pilaris and comedos should be somewhat modified. So far, in addition to the phrynoderma occurring in advanced vitamin A deficiency, only keratosis follicularis of Darier and pityriasis rubra pilaris have responded to vitamin A therapy. The occurrence of lichen pilaris in children is not common; it is encountered mostly during adolescence and adult life. It may be that in children lichen pilaris is an expression of vitamin A deficiency. The man presented by Drs. Bernstein and Goldberger shows no evidence of vitamin A deficiency in the scleral conjunctivas, but his sclerae show a much better blue color than one usually sees at his age. This cannot be the result of the vitamin therapy which he has recently received, since it has been shown by Kruse that it takes a much longer time for xerosis conjunctivae and Bitot's spots to disappear with vitamin A therapy.

DR. OSCAR LEVIN: It has been my experience that excellent results are obtained with vitamin A therapy in treatment of keratosis pilaris, pityriasis rubra pilaris and ichthyosis. I usually give 150,000 U. S. P. units of vitamin A daily. I have also observed good results when the vitamin is combined with calcium pantothenate. I believe the action of vitamin A is on the keratin-forming mechanism. In connection with the point brought out by Dr. Chargin as regards parapsoriasis and mycosis fungoides, the differential diagnosis should be emphasized. One often sees a dermatitis and questions whether it is going to be mycosis fungoides or not. Patients with parapsoriasis that develops into mycosis fungoides usually show lesions that are more elevated, exudative, crusted and pruritic and that frequently show a tendency to infiltration. In parapsoriasis en plaques the patches are not elevated and there is no infiltration, no pruritus and no exudation. The patches are more persistent and resistant to treatment and fre-

quently show a peculiar yellowish tint aside from a reddish or brownish color. Occasionally injections of pilocarpine hydrochloride and ultraviolet irradiation may prove of value in the treatment of parapsoriasis, while in the treatment of the so-called premycosis fungoides roentgen therapy will usually cause the disappearance of the lesions.

Dr. Eugene T. Bernstein: In the November issue of the Archives of Dermatology and Syphilology, O'Leary reported on the value of vitamin A therapy in the treatment of cutaneous diseases, and he arranged his therapeutic effects from 0 to 4. He stated that vitamin A is the most specific therapy for lichen spinulosus, and he gave it a score of 2 to 3 points. I want to emphasize that the man with mycosis fungoides never had pruritus or discomfort and had generalized lymphadenosis. On examining the patient we saw patches which were discrete, as today, just like macules, covered with branny scales, which I think should invariably be considered as characteristic of parapsoriasis. One other point concerning the woman should be mentioned: Excellent results were obtained from injections of liver extract, and it should be emphasized that she has had this disease for twenty years and today is in fairly good general condition.

Hodgkin's Disease of the Skin in a Negro. Presented by Dr. Oscar L. Levin.

H. G., a 32 year old Negro, was admitted to the Mount Sinai Hospital in September 1941, complaining of progressive swelling of the left side of the neck of three months' duration. The swelling interfered with motion of the neck and was associated with a loss of 15 pounds (6.8 Kg.) in weight. There was no cough, tendency to bleeding, diarrhea or eruption.

Examination revealed a well developed and well nourished Negro, in no distress. The pupils were round and regular and reacted to light. The fundi were normal. The left and right supraclavicular nodes were enlarged, matted together, firm and fixed. They were nontender and showed no evidence of underlying inflammatory process. The configuration of the chest was normal, and the lungs were clear. There was some widening of the mediastinum to percussion. The heart sounds were of good quality, and the blood pressure was 150 systolic and 75 diastolic. The abdomen was soft, and no masses or viscera were palpable.

The Mantoux test with a dilution of 1:1,000,000 gave a negative reaction. The sedimentation time was seventy minutes. The Wassermann reaction of the blood was 4 plus. The hemoglobin content was 86 per cent, and there were 13,000 white blood cells, with 74 per cent segmented and 16 per cent nonsegmented polymorphonuclear leukocytes, 8 per cent lymphocytes and 2 per cent monocytes. A guaiac test of the stool gave a 4 plus reaction, and the urine was essentially normal. Aspiration of sternal marrow revealed normal activity and normal cell distribution. The cerebrospinal fluid was normal. Roentgen examination of the chest revealed a large mediastinal mass extending both to the right and to the left. The lungs were not abnormal. Histologic examination of the left supraclavicular node showed the characteristic changes of Hodgkin's disease.

A course of radiotherapy was instituted, and the patient was discharged for continuation of this therapy. He has been under treatment in the outpatient department since then. The lesions in the chest have gradually shown a decreasing response to roentgen therapy, and the patient complains of increasing weakness. He has also been under treatment for syphilis but has been irregular in his appointments.

In January 1942, a group of pea-sized to quarter-sized firm tender nodules appeared on the chest over the manubrium sterni. These lesions gradually become confluent and the central portion superficially ulcerated. A biopsy performed at this time was reported as indicating Hodgkin's disease of the skin. The lesions responded at first to radiotherapy but gradually became resistant. At the same time numerous new nodules of a keloidal appearance developed around the original cutaneous lesion on the sternum as well as on the clavicular and axillary regions.

DISCUSSION

Dr. Charles Wolf: I have had the opportunity to observe this patient from a radiotherapeutic standpoint before he presented a dermatologic problem. I dare say few dermatologists would be able to say that the tumors were Hodgkin's disease. These lesions developed after systemic Hodgkin's disease appeared and the mediastinum was involved with pressure symptoms on the large bronchi. While the man was receiving treatment with high voltage roentgen rays for the mediastinal tumor, enlargement of glands in the neck developed, which was proved to be Hodgkin's disease. The erythrodermic form of the disease is encountered more frequently than the tumor form.

Dr. Howard T. Behrman (by invitation): In view of the lymphadenopathy and other constitutional changes of systemic Hodgkin's disease, I think I should say on examination of the lesions that they are suggestive of lymphoblastoma. Only when the disease became localized could one perform a biopsy and make a diagnosis of a specific member of the lymphoblastoma family, in this instance Hodgkin's disease.

Leukemia Cutis. Presented by Dr. Van Alstyne Cornell.

T. B., a man aged 57, was in good health prior to January 1941. At that time he noticed an erythematous papular eruption in both cubital areas, and the popliteal areas were involved in a similar manner one month later. By March the eruption had become generalized. Diffuse scaly lesions with induration of the skin were present, especially on the hands and the neck. In July the patient entered Bellevue Hospital and improved under treatment with mild ointments. After his discharge he entered Metropolitan Hospital, in October 1941, complaining of a generalized erythroderma with exfoliative dermatitis. Itching was present but was not severe. His condition improved with mild therapy consisting of baths and applications of ointments, and he was discharged to the City Home on Dec. 7, 1941. One week later he returned with an acute exacerbation accompanied by severe itching.

For two years prior to his admission the patient had worked as an attendant in a hospital for patients with tuberculosis.

The patient has a generalized eruption, most pronounced on the face and extremities. The skin is edematous, erythematous and thickened. There are fine scaly lesions on the scalp. On the chest and back and in the groins are many medium-sized red infiltrated papules. Many minute skin-colored shiny papules are also present. There is some fissuring as well as many infiltrated skin-colored papules and nodules on the extremities. There are single small cystlike lesions on the tongue, left hand and right thigh. The liver is

palpable 1 fingerbreadth below the costal margin, and small lymph nodes are palpable in the neck and axillas.

Examination of the blood gave the following results:

Date	Red Blood Cells, No.	White Blood Cells, No.	Polymorphonuclears	Lymphocytes	Monocytes	Eosinophils	Basophils
11/15/41	4,300,000	9,500	72	24	1	3	..
6/ 7/42	4,750,000	8,800	70	28	..	2	..
2/ 2/43	.....	19,000	19	59	2	12	2

The Wassermann and Kahn reactions of the blood were negative.

Date	Plasma Proteins	Fibrinogen	Albumin	Globulin	A/G Ratio
3/16/42	7.20	0.25	2.65	4.30	0.62
9/ 3/42	8.34	....	6.08	2.26	2.69

The urine was essentially normal, and roentgen examination of the chest revealed a normal cardiac shadow and no infiltration of the lungs. The first electrocardiogram gave evidence of myocardial damage, but two succeeding ones were normal. The basal metabolic rate was —17 per cent in November 1942 and +12 per cent in December.

Histologic examination showed an irregular acanthosis of the epidermis. In the corium there were numerous focal cellular infiltrations in what appeared to be the mesh of a reticulum. The cells were mostly lymphocytes, and, in addition, there were some small round cells and occasional wandering connective tissue cells. There were numerous thin-walled small blood vessels throughout the corium. The findings were suggestive of lymphatic leukemia. The biopsy was reported as revealing leukemia cutis.

Multiple Disseminated Sphaceloderma with Generalized Amyloidosis. Presented by DR. EUGENE T. BERNSTEIN and DR. LEWIS A. GOLDBERGER.

N. W., a man aged 33, is presented from Mount Sinai Hospital with an ulceration on the middle third of the right shin of three months' duration.

For the past sixteen years the patient has had repeated attacks of aches and pains with fever, polyarthritis and recurrent erythema-multiforme-like eruptions with ulcerations on various parts of the body. He has been hospitalized several times for from six to ten months at a time. While there, new outbreaks of eruptions appeared. The lesions were described as dull, soft, coppery red papules, lasting about three weeks, many of them then ulcerating. Ulcerations took from six to ten weeks to heal. Some lesions showed vesicle formation and were hemorrhagic. The liver and spleen were definitely palpable. Neurologic examinations gave normal results. A Rehfuss test meal showed total acid 52 and free acid 32.

On examination on several occasions the urine showed the specific gravity fixed at 1.010; it now shows only a faint trace of albumin. The blood pressure was 134 systolic and 60 diastolic. A blood count showed: hemoglobin content, 72 per cent, and white blood cells, 25,000, with polymorphonuclear leukocytes 87 per cent, lymphocytes 11 per cent and monocytes 2 per cent. The sedimentation time was ten minutes. The blood contained 14 mg. of urea, 11 mg. of calcium, 110 mg. of sugar, 230 mg. of cholesterol (esters 105 mg.), and 450 mg. of fibrinogen. The urea content of the blood was always normal. The blood did not yield organisms on culture, and the Wassermann reaction was negative. Puncture of vesicles yielded fluid containing many pus cells but no organisms, and culture of the material obtained produced no growth. A congo red test performed twelve years ago revealed a 10 per cent retention after one hour, and a month later no dye remained after one hour. One year later 30 per cent remained, and two years after that (nine years ago) repeated congo red tests showed a retention of 100 per cent. The Mantoux test was strongly positive with a dilution of 1: 100,000.

Roentgen examination of the chest revealed hypertrophy and mild dilatation of the right side of the heart, hypoplastic aorta and moderate elevation of the right side of the diaphragm. There was no abnormality of the lungs. Roentgenograms of the hands and elbows showed no abnormality of bone. Roentgenograms of the paranasal sinuses showed clouding of the right ethmoid and right maxillary sinuses; the frontal sinuses were large and the remaining sinuses clear. Roentgen examination of the knees showed slight arthritic changes of the knee joint, with no evidence of calcific deposits in the vessels.

A biopsy of the skin showed diffuse acute arteritis. A biopsy of a gland from the groin showed acute lymphadenitis. Examination reveals an irregular and ovoid ulceration on the right leg about 1½ by 3 inches (4 by 8 cm.) in size. The lower portion shows granulation, and the upper portion is deeply excavated with a clean floor. There are many dime-sized to hand-sized scars on the shoulders, back and upper and lower extremities and on the stump of the distal phalanx of the right index finger. There is also a large perforation of the nasal septum, the cause of which could not be explained by consulting otolaryngologists. There is macroglossia.

Histologic examination of tissue taken from this ulcer on Jan. 25, 1943 showed in one portion of the section considerable fibrosis, between the bundles of which are a few slightly dilated vessels. In another portion of the section were numerous small blood vessels, some with thickened walls and hyalinization. The matrix was loose and lacy, and there was a moderate amount of cellular elements. The microscopic diagnosis was granulation tissue of long standing in different stages of development.

DISCUSSION

DR. WILBERT SACHS: The term "sphaceloderma" is an old one. It is found in some of the oldest textbooks and in every modern textbook. Possibly the same etiologic factor is responsible for the amyloidosis and these ulcerative lesions, the amyloid itself not causing the lesions.

DR. E. WILLIAM ABRAMOWITZ: I do not think that the evidence presented is sufficient to support a diagnosis of amyloidosis. I should like to know if the term "sphaceloderma" will help one to understand the nature of the lesions any better than the term "pyoderma gangrenosum," which is now generally employed.

DR. LEO SPIEGEL: Has any one ever seen gangrene associated with amyloidosis? I presented a case of localized amyloidosis a few months ago before this section and reviewed the literature at that time. I found no mention of gangrene associated with this disease. It seems to be a coincidence, and I doubt that it has any connection with the amyloidosis.

DR. WILBERT SACHS: I saw a slide of one of the ulcerative lesions, and all I can say is that there is

granulation tissue, some early and some late. Multiple gangrenous areas are known as sphaceloderma.

DR. PAUL GROSS: If this disease were generalized amyloidosis, one would find no macroglossia. If, on the other hand, this patient was supposed to have a macroglossia, the case would belong in the group of cases of systematized amyloidosis, for which there is no clinical evidence. The cutaneous manifestations are those of a chronic pyoderma, and bacteriologic studies ought to be helpful in giving a clue for therapy.

DR. OSCAR LEVIN: None of the discussers have proved that amyloidosis is not present. The fact that there is such striking retention of congo red would indicate the possible presence of amyloidosis. In addition, the chronic suppurative lesions and the history of tuberculosis point toward the possibility of generalized amyloidosis. Ulceration may occur as a result of involvement of the small cutaneous vessels.

DR. EUGENE T. BERNSTEIN: This patient was observed for sixteen years at Mount Sinai Hospital by competent internists. A distinction should be drawn between generalized amyloidosis and systematized amyloidosis. In this case there is unequivocally generalized amyloidosis, proved by enlargement of the spleen, liver and kidneys; secondarily, a Paunz test was performed, which showed 100 per cent retention. This is most reliable. Amyloidosis is only a consequence of faulty protein metabolism and may be a result of syphilis, tuberculosis or a suppurative disease. Here is a man who has been observed for sixteen years, suffering repeated attacks of aches, pains, polyarthritis, erythema multiforme, etc. In generalized amyloidosis one never observes cutaneous amyloid of the lichenoid type; such amyloid is encountered only in systematized amyloidosis. Wilbert Sachs wrote an article on this subject in 1936 which was enlightening. He expressed the opinion that sphaceloderma may be caused by many things—for instance, by erythema multiforme and by inflammatory processes. The biopsy of the skin showed acute arteritis and a change in the vessel walls with hyalinization, but organisms were never obtained on culture. We do not know the underlying basis of the amyloidosis, but we think the fact that the Mantoux test with a dilution of 1: 100,000 gave a strongly positive reaction may indicate tuberculosis or periarteritis.

Arsenoresistant Syphilis? Pyogenic Ulceration? Destruction of Nose. Presented by DR. GIRSCH D. ASTRACHAN.

H. L., a man aged 31, was admitted to the Metropolitan Hospital Jan. 4, 1943, presenting a complete destruction of the nose and ulcerations on the adjacent parts of the face.

The patient was in the Navy from 1926 to 1928 and had been in Nicaragua, Panama, Cuba and many South American countries. From 1931 he received antisyphilitic therapy intermittently for several years. In October 1935 a "pimple" appeared on the septum, followed by an ulceration. From that time on he was treated in several different hospitals and dispensaries and antisyphilitic therapy was instituted. In spite of this, by the summer of 1936 the septum was entirely gone and the nose flattened. During the fall of 1936 the outer part of the nose began to undergo destruction, and by 1938 the nose was completely destroyed. The patient was treated with wet saline dressings for ten weeks, and the bridge of the nose, which was still present, healed under this treatment.

In September 1938, the bridge of the nose began to break down. In January 1939, the patient was given antisyphilitic therapy and the wound was washed daily. Zinc peroxide medicinal, the adhesive tape method, etc., were used. This seemed to improve his condition slightly. Fever therapy by injection was also employed in 1939, but he became worse and at that time lost his upper lip. The same year a sinus was found running back into the ethmoid and sigmoid sinuses. The bridge of the nose was removed and a radical ethmoid operation performed. All his teeth had been removed in 1939.

The patient claims that he had received injections of antimony and potassium tartrate and that these helped him somewhat.

The nose, including the septum and bridge, and the upper lip are completely destroyed. The destruction extends throughout the soft palate and part of the hard palate. Involving both cheeks and the lower part of the forehead, there is an irregularly shaped area of infiltration, ulceration and scarring. The patient presents ectropion of both lower eyelids, especially pronounced on the right side. The upper lids are edematous. The ulcerated areas are partly covered with a thick, grayish-yellowish purulent discharge.

The Wassermann and Kahn reactions of the blood were positive on three occasions. The urine was normal. A complete blood count was essentially normal except for a hemoglobin content of 60 per cent and the presence of 9 per cent eosinophils.

All smears contained streptococci and staphylococci. Culture was positive for Staphylococcus albus and aureus and for hemolytic streptococci. The blood chemistry was normal (sugar, creatinine, urea nitrogen).

DISCUSSION

DR. LEO SPIEGEL: The primary destruction of the nose and adjacent tissues is unquestionably due to syphilis. However, I believe there is now an accompanying secondary invader which is causing this severe destruction of the nasal tissues. Possibly the microaerophilic hemolytic streptococcus of Meleney may be the contributing factor, and the case should be investigated from that standpoint. Dr. Costello reported a similar case some months ago (*J. A. M. A.* **121**:36 [Jan. 2] 1943).

DR. MAURICE J. COSTELLO: By a process of exclusion, this patient may have the same type of infection from which my patient suffered, namely, microaerophilic hemolytic streptococcus infection causing destruction of the nose (*J. A. M. A.* **121**:36-37 [Jan. 2] 1943). About the time I was preparing my case for publication, I saw this patient at Bellevue Hospital and hoped to report his case also, but he left the hospital before he could be adequately studied and treated. The patient presented tonight has had prolonged antisyphilitic treatment without favorable effect on the lesions. The histologic diagnosis is a nonspecific inflammatory process and not syphilis; it is strictly symmetric. Therefore, I believe that his disease will eventually prove to be the type of infection to which I referred. A therapeutic test would be favorable response to zinc peroxide medicinal cream applied according to the proper technic. My patient was presented before the Manhattan Dermatologic Society twice, and all the members thought that the destruction of her nose was caused either by syphilis or by tuberculosis. I also gave my patient antisyphilitic treatment, without benefit. As soon as the clinical diagnosis was confirmed by the finding of microaerophilic hemolytic streptococci, zinc peroxide medicinal cream was used with success; the process was immediately arrested and finally cured.

DR. LEWIS B. ROBINSON: I presented this man about three years ago from Vanderbilt Clinic, and at that time the consensus was that syphilis had nothing to do with the process. I put him into the hospital, where the rhinolaryngologists removed a great deal of necrotic bone, and he was treated for syphilis for a long time. We also used zinc peroxide medicinal and sulfonamide compounds, and the lesions practically healed, with the exception of one little spot in the nose. He was also given iodides. I suggest that a roentgen examination of the shoulder be made, as there is an interesting lesion on the humerus.

DR. GEORGE M. LEWIS: At New York Hospital, where the patient was studied for several weeks, a diagnosis of leishmaniasis was considered because of the history of onset in South America, the destructive character of the disease and the fact that while the patient has syphilis the disease process has not responded to antisyphilitic therapy. Our observations contributed little to the further diagnosis, and we found no evidence that leishmaniasis played a role. Dr. Howard Fox saw the patient and felt that syphilis was the most probable cause for the massive destruction now present. Cultures did not at any time show organisms to support the theory of a microaerophilic streptococcus infection.

DR. E. WILLIAM ABRAMOWITZ: I am reminded of a patient with arsenic-resistant syphilis presented a few years ago, a man beginning to have destructive lesions on the face involving the nose and mouth. He had received malarial treatment for syphilis in an early stage of the disease and evidently had not had sufficient quinine to cure the malaria. When this was given, he responded to the arsenicals and the ulceration healed. The patient presented by Dr. Astrachan was in the tropics and may have gangosa. If a microaerophilic streptococcus is present, zinc peroxide medicinal is indicated. If gram-positive bacteria are present, gramicidin or penicillin may prove effective.

DR. PAUL GROSS: This case is closely related to the case presented by Drs. Bernstein and Goldberger as one of sphaceloderma. The recent paper by Dr. Costello and the discussion by Dr. Frank Meleney draw a clear picture of these chronic pyogenic infections and the bacteriologic factors involved. Their unusual feature is the fundamental fact that they represent chronic infectious granulomas of the skin due to pyogenic organisms, in contradistinction to all of the other cutaneous manifestations due to streptococci and staphylococci, which are always acute, at least as far as the primary lesion is concerned. In addition to the specific organism demonstrated by Dr. Meleney, I believe predisposing factors contributed to the development of this chronic sensitization. Ulcerative colitis has been well known to be one of the factors, but the role of chronic osteomyelitis as a predisposing cause has not been sufficiently stressed. Several times I have observed chronic disseminated pyoderma developing in patients with osteomyelitis. The lesions were located at sites remote from the bones affected by the osteomyelitis.

DR. GIRSCH D. ASTRACHAN: I presented this patient because of the uncertainty of the diagnosis and mainly for suggestions as to therapy. My impression is that this man has tertiary syphilis combined with the type of infection described by Dr. Costello (Microaerophilic Hemolytic Streptococcus Infection Causing Destruction of Nose, *J. A. M. A.* **121**:36 [Jan. 2] 1943). The fact that this patient did not respond to antisyphilitic therapy does not exclude the possibility of tertiary syphilis. All dermatologists know of the existence of cases of this kind. A photograph of a man with destruction of the face similar to that of this patient is shown in an article by H. Cole and associates (Cole, H.; Driver, J. and Freeman, H.: Syphilis of the Center of the Face, ARCH. DERMAT. & SYPH. **43**:943 [June] 1941). The present patient was treated years ago with arsenicals and a severe jaundice developed. The treatment was discontinued temporarily and when resumed was irregular for a while. That may be the cause of the resistance to arsenicals. I do feel, however, that microaerophilic hemolytic streptococcus infection should also be considered, because according to the patient his eruption improved somewhat when zinc peroxide medicinal was used. I do not believe that iodides have been used. Leishmaniasis was considered as a diagnosis but was excluded by microscopic examination.

Melanoma: Regression with Roentgen Ray Therapy. Presented by DR. OSCAR L. LEVIN.

J. T., a man aged 72, was admitted to the Mount Sinai Hospital in August 1942, complaining of a painful ulceration on the right sole of sixteen months' duration. This lesion was first noticed as a dime-sized slightly elevated bluish nodule which rapidly enlarged and then ulcerated. The past history is irrelevant.

Examination in August 1942 showed a palm-sized superficial ulceration of the right foot. Small islands of granulation tissue and a few pea-sized bluish nodules were interspersed throughout the ulcerated area. The border was serpiginous and dark blue. Histologic examination revealed the presence of melanocarcinoma. Amputation was advised, despite the age of the patient, but was refused. As a palliative measure, radiotherapy was instituted. The lesion received 5,800 r in doses of 200 r to the entire area every four or five days. The formula employed was 140 kilovolts, 2 milliamperes, no filtration and a focal skin distance of 30 cm. The lesion regressed with such rapidity that the diagnosis was questioned. Another biopsy was performed on Oct. 11, 1942. The lesion was again reported as melanocarcinoma. It has continued to decrease in size. At present, there is but one bluish nodule 0.5 mm. in diameter in evidence.

LOS ANGELES DERMATOLOGICAL SOCIETY

F. L. X. WILHELM, M.D., *President*

A. FLETCHER HALL, M.D., *Secretary*

April 13, 1943

A Case for Diagnosis (Parapsoriasis [Haberman]?). Presented by DR. H. C. L. LINDSAY.

Mrs. W. W., a 45 year old white housewife, states that she had eczema as a child and "ulcers on her legs" when she was 14 years of age. Her present eruption, however, consists of a discrete rash on her body and arms. The lesions are scattered on the body almost like a mild form of scabies, but the individual lesions are mostly macules, slightly pigmented and of the size of large freckles. There is some suggestion of lichen-like papulation, and grouping is evident on the arms. There is a definite urticarial factor in the rash. The skin flushes easily with a blotchy macular erythema. She has frequently had herpes on the nose and lips, and there has been a palmar scaling dermatitis for years.

The Wassermann reaction of the blood was negative in 1942, and the patient states that gastric analysis revealed achlorhydria. The blood count was normal, with eosinophils varying from 1 to 4 per cent. The sedimentation rate was normal.

A biopsy showed minimal changes: moderate hyperkeratosis but no acanthosis and some foci of round cell infiltration about the blood vessels of the derma but no hyperemia or edema.

DISCUSSION

DR. SAUL ROBINSON: I agree with the diagnosis.

DR. SAMUEL AYRES JR.: I suggest the possibility of urticaria pigmentosa in this case. I thought the lesions had the color and appearance characteristic of it. There was no apparent scaling or other changes in the lesions except the discoloration. The patient said they stood out a little when she exercised or got warm.

DR. CHRIS HALLORAN: I agree with the remarks of Dr. Ayres. When the skin was stroked, the lesions became more prominent. Search for mast cells in a biopsy specimen should determine whether or not the eruption is urticaria pigmentosa.

DR. H. C. L. LINDSAY: I took into consideration urticaria pigmentosa at first, but the microscopic section proved that the disease was not that. Mast cells are not present in sufficient quantities to justify that diagnosis.

Kraurosis Vulvae. Presented by DR. PAUL D. FOSTER and DR. MOLLEURUS COUPERUS (by invitation).

Mrs. M. W., a 70 year old white woman, has always been in good health and robust, except for a mild cystitis, which was cured, and for a polyp removed from the uterus eighteen years ago. When first seen, in February 1938, she complained of severe itching of the vulva and perineum of ten years' duration. During the preceding twelve months there had been considerable inflammation in the perineal region.

At the present time she shows complete loss of the labia majora and minora, with great thickening of the adjacent tissue, which has a grayish dry and hard appearance. The whole area appears leukoplakic. About eighteen months ago a squamous cell epithelioma about the size of a dime developed on the perineum; this was removed, and radium was applied. The Wassermann reaction of the blood was negative.

DISCUSSION

DR. H. P. JACOBSON: I am not impressed with the diagnosis of kraurosis in the present case. The presenting picture is cutaneous atrophy associated with telangiectasia. It seems to me that this is a radiation dermatitis associated with atrophy and telangiectasia.

DR. SAMUEL AYRES JR: I should like to ask Dr. Foster, in answer to Dr. Jacobson's remarks, if the radiation was given after the onset of the malignant changes and if any endocrine therapy has been given. The patient said that at first she had intolerable itching and that it later disappeared. Was this due to use of an estrogenic substance?

DR. PAUL FOSTER: When she was first seen, the mucous membrane portion of the external genitalia was hard, dry, thick and somewhat grayish. The greater portions of the labia majora and labia minora were atrophic. When she came in, she was given injections of whole ovarian extract in rather large doses over a period of two years. At that time, we gave her around 4,000 r of roentgen rays, 150 r at weekly intervals. The area which had been hard and leukoplakic gradually became soft. Then about one and a half years ago a proved squamous cell epithelioma developed in the perineum. This was removed and radium applied. The result so far is good. The woman was suffering intolerable itching when she came, and after about four months of treatment with roentgen rays and whole ovarian extract it entirely subsided. Dr. Couperus and I have had 2 patients with kraurosis vulvae which responded in the same way to the same treatment.

A Case for Diagnosis (Lupus Erythematosus?). Presented by DR. CLEMENT E. COUNTER.

V. R. S., a 53 year old white man, first noticed a vesicular lesion on the left cheek in November 1941; this became crusted and during April and May 1942 was treated with 6,000 r of roentgen irradiation to an area about 1 cm. in diameter. Soon after the reaction to the radiation was healed, vesicular lesions appeared around the treated area.

The patient now shows a circumscribed oval patch about 4 cm. long by 3 cm. wide on the left cheek just anterior to the ear. Near its middle is a smooth atrophic area about 6 mm. in diameter. The rest of the lesion is composed of extensive vesicle formation from which little fluid evacuated when pierced. No other similar lesions are present elsewhere

The blood count was normal, and the Wassermann reaction of the blood was negative.

DISCUSSION

DR. KENDAL FROST: Without a biopsy one cannot be sure about this lesion. It may be lupus erythematosus or a superficial cicatrizing epithelioma.

DR. CHRIS HALLORAN: I agree with Dr. Frost's remarks.

DR. SAMUEL AYRES JR.: I gathered from this history that the lesion first appeared in the form of a bleb and has taken its present form since, which would raise the possibility of an eruption due to phenolphthalein or some other drug.

DR. A. FLETCHER HALL: There is a history of its having been vesicular or having vesicles or bullous lesions, and, although it would be difficult to make any diagnosis now without a biopsy, I should like to suggest the diagnosis of the Senear-Usher type of pemphigus.

DR. CLEMENT COUNTER: I should like to make clear that the roentgen treatment was localized to a much smaller area than the lesion presently occupies. Originally it was a crusted vesicular lesion, which led a diagnosis of epithelioma, which, in turn, led to localized destructive roentgen therapy and the present atrophic condition. Most of the lesion has not been exposed to irradiation. On many occasions I have observed the presence of large vesicles. The entire erythematous patch is at times almost one vesicle. The vesicles contain serosanguineous fluid.

NOTE.—A biopsy showed changes consistent with a diagnosis of the Senear-Usher type of pemphigus. The lesion has shown great improvement after treatment with gold sodium thiosulfate.

Chancriform Penile Lesions. Presented by DR. H. C. L. LINDSAY.

Mr. C. H. was presented at the March 1943 meeting of the Los Angeles Dermatological Society. At that time it was brought out that (1) repeated dark field examinations showed no spirochetes; (2) stained smears showed none; (3) no Ducrey bacilli were seen; (4) no Crassus bacilli were seen; (5) no Donovan bodies were seen; (6) no adenopathy was demonstrable within the pelvis or in regional glands; (7) no rash was seen. The patient feels well, and the chancriform lesions are gradually healing. Soaks in potassium chlorate solution were used, but the patient is using "camphor ice" on his own initiative. His wife is well. The Wassermann reaction was negative.

Positive findings included: a weakly positive Frei reaction and an unidentified diplococcus larger than the Neisser organism.

Biopsy material, prepared by the Krajian method (Krajian, A. A.: A Rapid Method of Staining Spirochaeta Pallida in Single Sections of Tissue, ARCH. DERMAT. & SYPH. **32**:764-767 [Nov.] 1935) shows one well defined spirochete, identified as Treponema pallidum.

DISCUSSION

DR. IRVING BANCROFT: I understand that only one spirochete has been found in the sections. Then the only question is, Why is it that there has not been a positive Wassermann reaction by this time? I think it would be a good idea to wait and see whether the Wassermann reaction becomes positive.

DR. H. P. JACOBSON: I seriously question the diagnosis of syphilis. While I have never seen this patient before, the presenting picture tonight is neither that of chancre nor that of chancroids. The lesions are ulcerations undergoing involution, and scarred healing associated with elevated somewhat infiltrated borders is present. Regional inguinal adenopathy is entirely absent. There is no cutaneous exanthem. The patient has no complaints and presents no symptoms. The serologic reaction of the blood is completely negative. In view of these considerations, the best that one can do is submit the diagnosis of granuloma the exact cause of which has thus far not been established.

DR. PAUL FOSTER: I have seen 2 patients with lesions that looked like this clinically, lesions on the penis which were hard and waxy and of a yellowish tint around the edge. Biopsy of a section of each showed conditions typical of granuloma annulare. They were treated with solid carbon dioxide. I saw 1 of the patients later and he was entirely well. The histories were almost identical with that of the present patient, and the Wassermann reaction was also negative.

DR. SAMUEL AYRES JR.: There is an interesting possibility in this case: The lesions may be gummas, which can, of course, occur with a negative serologic reaction. That point can be cleared up by histologic studies.

DR. H. C. L. LINDSAY: One of those chancres could not have been more suitable for clinical demonstration of a hard chancre if it had been made to fit a textbook description.

A Case for Diagnosis (Early Stage of Idiopathic Atrophy?). Presented by DR. M. E. OBERMAYER and DR. SAUL ROBINSON.

C. G., a 53 year old white housewife, complains of cutaneous changes of five years' duration, which, however, have caused no symptoms except that the involved areas become slightly livid when she exercises.

Examination now reveals macular areas varying in size from 2 to several centimeters in diameter and of irregular somewhat oval shape on the posterior side of the right thigh, anterior side of the left thigh, flexor surface of the right forearm and upper part of the back. The lesions are perceptible by a slight change in color, livid at the periphery and somewhat paler in the center, which gives a faint suggestion of an annular configuration.

Microscopic examination of a specimen removed from the right thigh revealed a normal epidermis; the collagen was edematous and somewhat homogenized, and the nuclei of the connective tissue were increased in number. There was distinct vascular dilatation, but the number of lymphocytes which surrounded the blood vessels was too small to be called a perivascular infiltration. The appendages appeared normal.

DISCUSSION

DR. SAMUEL AYRES JR.: I agree with the diagnosis of idiopathic atrophy. I do not think it is the same as morphea. This lesion has no infiltration, and infiltration seems to be one of the essential qualities of morphea.

DR. M. E. OBERMAYER: My first clinical impression was that the lesions represented a localized disturbance of vascular development related to the group of diseases of which nevus anemicus is best known. When Dr. Robinson examined the patient, he thought immediately of an early stage of poikiloderma; I cannot help admiring his diagnostic acuity, as no evidence of atrophy was detectable clinically. However, subsequent microscopic examination has revealed changes which may well represent the earliest stage of one of the idiopathic atrophies, such as poikiloderma.

Keratosis Pilaris of the Face. Presented by DR. NELSON PAUL ANDERSON.

C. R. is a 3½ year old white boy. The present eruption was first noticed on the face when he was 8 months old. It has remained confined to the face except for a short time at the age of 1½ years, when there was some similar involvement of the arms and shoulders.

At present the entire face, especially the cheeks and the center of the forehead, presents a papular follicular eruption composed of small whitish papules. Numerous small reticulated pitted atrophic scars are present. The surface of the cheeks has a more or less nutmeg grater feel to the palpating finger.

Examination of the follicular plugs under the microscope reveals the presence of minute hairs.

DISCUSSION

DR. SAUL ROBINSON: I agree with the diagnosis as presented, but I was thinking of the possibility of avitaminosis A. I should like to see this boy again after he has received treatment for avitaminosis A.

DR. NELSON PAUL ANDERSON: This case was interesting to me for two reasons. First, I have seen 2 other young children with a similar eruption, both of them members of the same family. Second, the striking feature is that there is a reticulated atrophy. One does not associate keratosis pilaris with atrophic changes in the skin. The only information I have been able to get is that Ormsby's text contains the statement that Tilbury Fox many years ago presented some patients with keratosis pilaris of the face with concomitant atrophy. The youngster is at present taking large doses of vitamin A, but not enough time has elapsed to tell whether or not there are any changes in the eruption.

Urticaria Pigmentosa. Presented by DR. CLEMENT E. COUNTER.

J. S., a 26 year old white woman, first noticed three spots on one thigh in 1935. Soon others appeared on both thighs and arms, and then lesions began to appear on the trunk. Sometimes they seem to be redder than at other times, the variations occurring within a week. The lesions present are about 3 to 5 mm. in diameter. They are brown to red; the brown lesions are macular, while some of the red lesions are papular. The trunk, thighs and arms are involved. A mild seborrhea was also present last month.

A blood count showed: hemoglobin content, 60 per cent (10.2 Gm.); red blood cells, 4,440,000 and leukocytes, 7,900, with polymorphonuclear leukocytes 57 per cent, lymphocytes 36 per cent, mononuclear leukocytes 2 per cent and eosinophils 5 per cent. The Wassermann reaction of the blood was negative, and urinalysis revealed normal conditions.

DISCUSSION

DR. KENDAL FROST: I have a patient with urticaria pigmentosa whom I have seen over a period of twenty years who had profuse lesions at one time. With no treatment the lesions have gradually almost disappeared.

A Case for Diagnosis (Pemphigus Erythematosus?). Presented by DR. PAUL D. FOSTER and DR. MOLLEURUS COUPERUS (by invitation).

B. M., a 42 year old white woman, had eczema as a child. In 1938 she had a thyroidectomy and in 1942 a hysterectomy. Her present eruption started two years ago on the chest as a "pimple"; it has never been oozing. The right shoulder became involved six months ago. The lesions have been pruritic from the start.

She now presents a violaceous-erythematous papular eruption, almost nodular, in confluent patches varying in size from that of a dime to that of a half-dollar, with circinate borders, dry and in some areas rather scaly. The eruption is limited to the upper part of the chest, over the sternoclavicular articulations. On the posterior aspect of the right shoulder there are some individual papular lesions, all of which are excoriated.

The blood sugar level was normal; the blood count and urine were normal, and the Kahn and Kline reactions were negative.

DISCUSSION

DR. M. E. OBERMAYER: When examining this interesting patient, three diagnostic possibilities came into my mind: (1) localized dermatitis herpetiformis; (2) pemphigus erythematosus, and (3) familial benign chronic pemphigus. I think that the microscopic slide showed the dyskeratotic cells characteristic of the rare disease variously termed familial benign pemphigus, recurrent herpetiform dermatitis repens, bullous Darier's disease and dyskeratosis bullosa hereditaria. I favor the last-named designation and should like to point out that the disease is not always familial or hereditary. In a patient who was under my observation in Chicago no familial or hereditary features could be detected, and I understand that none are present in this woman.

DR. H. C. HALLORAN: I have a patient with chronic benign familial pemphigus that I have followed for a period of five years, and no other members of the family are affected.

DR. SAMUEL AYRES JR.: In regard to Dr. Obermayer's remarks about familial pemphigus, the disease which the Haileys described is the same that Dr. N. P. Anderson and I described under a different name, and it does not show any similarity to the disease of this woman. I think that in most of the cases which the Haileys, Dr. Anderson and I reported the eruption had a tendency to occur on the sides of the neck, in the axillas and on flexor surfaces. There were moist surfaces that gradually spread peripherally and would subside and flare up again as a spreading moist condition. I understand that this woman's lesions have been present most of the time in this particular area and on her back. From the clinical observation I thought of an atypical form of lupus erythematosus resembling that of a patient I showed at the last meeting, one whose lesions resembled impetigo and proved to be lupus erythematosus.

DR. W. H. GOECKERMAN: I thought the patient definitely had lupus erythematosus. She had a few lesions on the side of the neck that I thought were typical.

DR. C. RUSSELL ANDERSON: Ordinary discoid lupus erythematosus can start as vesicular and bullous lesions. The patients may be first treated for impetigo. I support Dr. Ayres' remarks.

DR. STANLEY CHAMBERS: I agree that the lesions on the side of the neck were typical of lupus erythematosus.

DR. PAUL FOSTER: When this woman first was seen Dr. Couperus and I thought she had seborrheic dermatitis. We treated her for about two weeks, but nothing happened. Then we performed a biopsy, and it proved that the disease definitely was not seborrheic dermatitis; for that matter, it was not lupus erythematosus either, although when we took the specimen for biopsy we were thinking of the Senear-Usher type of pemphigus. After listening to the discussion, I should be more likely to agree with Dr. Obermayer on the diagnosis.

Lupus Erythematosus. Presented by DR. PAUL A. FOSTER and DR. MOLLEURUS COUPERUS.

H. R., a 42 year old white man, has had considerable trouble with sore throat and tonsillitis. About six weeks ago he noticed an eruption on his scalp and soon afterward also on his face. He now presents a number of bright erythematous nodular lesions on the sides of the face and at each side of the nose, varying in size from that of a split pea to that of a quarter. Some of the lesions show a central depressed area with some scaling.

A blood count showed 4,380,000 erythrocytes and 3,700 leukocytes, with 38 per cent polymorphonuclear leukocytes, 52 per cent lymphocytes, 4 per cent mononuclear leukocytes and 6 per cent eosinophils. The hemoglobin content was 92 per cent. The urine was normal, and the Wassermann reaction was negative.

Lupus Erythematosus with Involvement of the Conjunctiva. Presented by DR. NELSON PAUL ANDERSON.

Mrs. C., a young Mexican woman, who presents a typical discoid lupus erythematosus involving the face, is presented for two reasons: First, there is involvement of a small region of the palpebral conjunctiva of the right lower eyelid. In this erythematous glazed-appearing area definite stippling can be seen. Second, she gives a definite history of complete remission of the disease during a recent pregnancy.

DISCUSSION OF CASES OF LUPUS ERYTHEMATOSUS

DR. CHRIS R. HALLORAN: I thought the case with involvement of the conjunctiva, presented by Dr. Anderson, especially interesting. This woman was a patient of mine at the

Los Angeles County Hospital a few years ago. During pregnancy the lesions of lupus cleared and remained away during lactation. Later they recurred.

DR. SAUL ROBINSON: Dr. Foster's patient has had lupus erythematosus for about six weeks, and the lesions are raised and inflammatory. He has a history of recurrent pharyngitis and septic tonsils. I think that this would be a good case in which to use a sulfonamide compound. Probably there is a focus of infection underlying this eruption of lupus erythematosus.

DR. SAMUEL AYRES JR.: I think sulfanilamide would be effective to bring the acute condition under control, but the patient ought to have his tonsils removed. Incidentally, Dr. Anderson's patient had a badly decayed molar, which probably is another contributing factor.

Epidermodysplasia Verruciformis. Presented by DR. NELSON PAUL ANDERSON.

N. A., a young white woman, states that her present eruption has been present since birth. On the dorsum of the left hand and the back of the fingers are twenty to thirty single and grouped erythematous, flat-topped, slightly raised papular lesions. At first glance the lesions are suggestive of flat warts, but against such a diagnosis is the duration of the eruption, its failure to spread and the size of some of the larger lesions.

DISCUSSION

DR. M. E. OBERMAYER: I want to express my thanks to Dr. Anderson for presenting such a rare disease, which I should not have been able to recognize.

DR. NELSON PAUL ANDERSON: I have always been interested in this disease. I have been trying, without success, to trace my original patient.

Epitheliomas with Spontaneous Involution. Presented by DR. SAMUEL AYRES JR.

I first saw G. A. B., a 60 year old white man, eighteen years ago. At that time he had a lesion which had been present about three weeks and which was located on the upper side of the nose; it consisted of a rounded nodule perhaps a little larger than a cherry seed, covered by an easily detachable dry crust or scale, which was probably caused by a freezing treatment which had been given three days previously. The lesion was characteristic of basal cell epithelioma and responded to treatment with moderate doses of radium. The patient at that time stated that he had had two similar lesions elsewhere on his nose, one of which had been treated by excision and the other by cautery. Since then he has been observed on a number of occasions with lesions on various parts of the face which were clinically typical of epitheliomas, either of basal or of squamous cell type. The patient has made the observation on a number of occasions, however, that he has had a number of such lesions which have disappeared spontaneously.

The patient was observed yesterday for the first time in ten years. He stated that during these ten years he had had at least six lesions which in a number of weeks had developed into what he is now familiar with as an epithelioma and which then suddenly disappeared without treatment. The present lesion began about three or four weeks ago, and the patient feels it is now beginning to subside, even though it has not had any treatment.

Examination reveals on the outer portion of the right nostril an approximately pea-sized rounded nodule showing central corneous scaling or plugging suggestive of a prickle cell epithelioma. He presents numerous scars scattered over his face where former lesions have been treated.

Tissue has not been taken from the present lesion for biopsy. A biopsy report on April 15, 1939 stated: "Tissue from the right side of the upper lip reveals Broder's epithelioma of the lip, approximately of grade II."

DISCUSSION

DR. M. E. OBERMAYER: I disagree with the diagnosis and suggest that the lesions are artefacts. The patient admitted manipulation and told me how he picked small pieces from the ulcers. It was stated in the history that at one time a microscopic diagnosis of squamous cell epithelioma of the lip was made from a lesion which later healed spontaneously. While from time to time one sees spontaneous healing of basal cell tumors, no such occurrence in a squamous cell epithelioma of the lip has ever come to my attention. I should rather assume that the histopathologist who examined the specimen mistook a pseudoepitheliomatous hyperplasia for a true epithelioma. The histologic features of pseudoepitheliomatous hyperplasia may be encountered in specimens from the border of any ulcer of long standing, and differentiation is at times extremely difficult, as was recently pointed out in a paper by Dr. Mercer and myself (*J. A. M. A.* **118**:139-140 [Jan. 10] 1942).

DR. CHRIS HALLORAN: Clinically the lesions suggest tertiary syphilis to me.

DR. W. H. GOECKERMAN: This was one of the most interesting cases of the evening. I have certainly never seen anything akin to these lesions, if they really are spontaneously healing epitheliomas. I, too, tried to elicit a history suggestive of self-inflicted lesions, but I could not fully satisfy myself. Still, I believe most of the lesions are self inflicted. If they are spontaneously healing epitheliomas—and I do not for a moment deny such a possibility—where can one find anything akin to this reported in the literature? These epitheliomas are supposed to occur at intervals over many years, only to heal spontaneously; if such can be

proved to be a fact, the case should be reported; but a further report certainly is not warranted on the evidence presented tonight, nor on the basis of one biopsy. Whether one of the original lesions was an epithelioma, I do not know. Aside from this, I disagree with the diagnosis as presented.

DR. H. C. L. LINDSAY: The lesion on the right ala nasi was like a spot of acne necrotica, as was also a lesion on the scalp.

DR. H. P. JACOBSON: Dr. Ayres's case I view as the most interesting presentation of the evening. I confess I have never seen a spontaneously healed epithelioma of any kind, and the case presented is certainly unusual and rare. I cannot subscribe to the views expressed that the pitted scars are a result of artificially produced lesions. Close examination of the scars reminds one of the cicatrizing type of epithelioma, which is characterized by slow evolution and a rather low degree of malignancy. One hyperkeratotic lesion on the left side of the face shows some infiltration and is definitely suggestive of an epithelioma. While one cannot be certain without additional microscopic study of tissues involved that the scars are a result of preexisting epitheliomatous lesions, the suspicion that they are is rather strong.

DR. SAMUEL AYRES JR.: My feelings are a little bit hurt at the implication that I am not a good observer. For a good many years this patient has had unquestioned epitheliomas from a clinical point of view. Most of the scars are where lesions have been treated by me and by others. Dr. Percy removed one from the lip, where the large scar was, which showed a grade II prickle cell lesion. I have seen the patient over a period of ten or fifteen years with basal cell and prickle cell lesions. Not all of these were treated by radium or cautery; on several occasions there were lesions which cleared spontaneously. This present lesion seems to have reached a peak and is apparently beginning to subside. I am thoroughly sympathetic with the idea of the rarity of self-healing epitheliomas.

NOTE.—Biopsy of superficial layers taken from part of the lesion in question showed changes suggestive, but not completely characteristic, of squamous cell epithelioma of grade I. The lesion was practically imperceptible when observed on July 3.

Lichen Planus of the Gums. Presented by DR. NELSON PAUL ANDERSON.

Mrs. V. M. F., a 35 year old white woman, states that her present complaint began seven years ago and has remained confined to the gums. She presents a definite reticulated lacy network of lichen planus involving the tips of the gingival papillas.

A biopsy was performed at the Mayo Clinic three or four years ago by Dr. Hamilton Montgomery. Preparations of gold, of bismuth and of arsenic as well as vitamins have been given as treatment, without benefit.

DISCUSSION

DR. SAUL ROBINSON: I agree with the diagnosis. I never saw lichen planus localized to the gum tissue. Regarding the response to therapy, I do not think the prognosis for clearing is good.

DR. CHRIS HALLORAN: I agree with Dr. Robinson's remarks. The problem is what to do for patients with lichen planus of the mucous membrane of the mouth. It is my experience that such lesions do not respond to any form of therapy.

DR. C. RUSSELL ANDERSON: Lichen planus of the mucous membranes of the mouth has been erroneously diagnosed and treated as submucous thrush by some physicians.

DR. KENDAL FROST: Dr. Nelson P. Anderson, I think, presented a patient a couple of years ago with lichen planus of the gums, and since then I have seen 3 women with lesions of lichen planus most evident on the gums. One had lesions limited to the gums while the others had oral lesions also. All were extremely resistant to treatment. All three women had more erosions than ulcerations, and they were severe and painful. Interestingly, 1 woman was young, another was in her early forties and the third was an elderly woman who lived alone. I have seen the last patient over a period of two or three years; she brought her sister in one day and said she thought the sister also had the disease. The sister did have typical lichen planus lesions on the tongue.

DR. NELSON PAUL ANDERSON: This is the first case of lichen planus I have ever seen in which the lesions were limited to the gums. I have seen patients with severe lesions which also involved the mouth and lips.

Hydroa Estivale with Secondary Cutaneous Changes. Presented by DR. SAMUEL AYRES JR.

R. F. is an 8 year old white boy. His present eruption began about five years ago and has been present more or less continuously ever since; it is especially severe when he is exposed to the sun. The disease was first noted at the age of 3 years, when lesions which were thought to be infections appeared on his hands. The disease has always been worse during the summer, but it has also occurred in winter when he was exposed to sun and wind. The mother states that vesicles and blebs develop on the affected areas.

The eruption is mainly confined to the dorsal aspects of the hands and wrists, the face, the ears and the back of the neck. There are no blebs seen at the present time, but there is some crusting on the face and hands. Secondary changes of the skin consist of thickening and scaling, with a brownish pink discoloration. The extensor aspects of the arms show a

growth of hair decidedly in contrast to the hair on the covered portions of the body. The patient has several badly infected teeth, and the mother stated that since early childhood his teeth have had a tendency to decay.

It is proposed to remove the infected teeth on the possibility that the photosensitivity may be the result of a focus of infection and to administer calcium and vitamins.

DISCUSSION

DR. PAUL FOSTER: I have seen this boy several times. The clinical picture resembles hydroa estivale. I think I have seen only 2 patients with a similar picture here in California. This boy's eruption starts with a sort of whitish pinhead-sized macule, perhaps 1 mm. in diameter, with a red areola around it. Later the whitish macule becomes yellow, the areola becomes a wheal and the central portion becomes hemorrhagic while the outside becomes yellowish or pearly and translucent. Then in about two weeks crusts form and fall off. Sometimes the lesions coalesce. This particular eruption instance represents the mutilating type of hydroa estivale; it leaves scars because of the deep involvement. We have asked for a test of the urine for porphyrin.

DR. KENDAL FROST: I saw 1 case of an eruption similar to this in a small boy. I saw him only twice and never in a period of active lesions. He, however, had lesions on the ears and hands resembling those of this boy. A biopsy of these lesions showed the disease to be colloid degeneration, probably secondary to the repeated attacks of what corresponded in the history to hydroa estivale.

DR. W. H. GOECKERMAN: I think the eruption is a classic one of hydroa estivale. My personal reaction is that it is mild. One sometimes sees such lesions in severe form. The boy is at an age at which I think he may get over the worst part of it. The advice I always give to patients with hydroa estivale is to keep in mind that they cannot tolerate sunlight well and that they must choose an occupation that keeps them away from sunlight as much as possible. Some local application to protect against sunlight can be given, but is not satisfactory as a rule. When the disease is severe, it becomes a serious affair.

DR. CLEMENT COUNTER: From talking with the mother, it was learned that little is being done to protect this child from the sun.

DR. SAMUEL AYRES JR.: The secondary changes in the skin are interesting. There are thickening and discoloration. Dr. Frost remarked that it might be colloid degeneration. On the arms there is an excessive growth of hair, evidently nature's attempt to protect the skin. The boy has four or five badly decayed teeth. The teeth never were good. This brings up the question as to whether the dental decay is part of the same disturbance, perhaps a disturbance in calcium or phosphorus metabolism. I think the decay of the teeth is a metabolic disturbance related to the photosensitivity. It would seem that rather careful metabolic studies and adequate vitamin therapy would be in order.

Poikiloderma Atrophicans Vasculare. Presented by DR. CLEMENT E. COUNTER.

A. S., a 69 year old obese white woman, has suffered from her present eruption for eight years. At the onset, there was severe nocturnal itching; this has been much less severe for the past four years, however. The skin has a great tendency to wrinkle in sharp ridges. Certain large patches under the arms, on the adjacent portion of the chest and on the breasts are deep brown and pigmented. Similar patches occur on the abdomen and thighs. In the depths of the folds, as in the groins, under the arms and under the breasts, the skin is free of lesions. The deposits of pigment are in a variegated reticulated pattern.

This patient also suffers from hypertensive heart disease, with a left ventricular type of cardiac enlargement. The blood count and urine were normal, and the Wassermann reaction was negative.

DISCUSSION

DR. W. H. GOECKERMAN: I still hold that the poikiloderma atrophicans vasculare as first presented by Jacobi is a rare and distinctive disease of the skin. Poikiloderma of Civatte and Oppenheim is another matter and covers a multitude of eruptions so far as I can determine. In fact, I do not see much use for this mellifluous term for the latter eruptions. They may represent anything from the lymphoblastomas, disseminate lupus erythematosus and the still not understood atrophies of a certain type to a somewhat unusual picture of eczema.

DR. PAUL FOSTER: I have observed in this case that the areas gradually became violaceous or purplish. The itching receded, and they began to take on a telangiectatic appearance. Then the lesions became brownish, surrounded by white atrophic scars. When I saw the patient, she showed signs of mycosis fungoides.

DR. CLEMENT COUNTER: My main reason for presenting this patient is that she has a most extraordinary type of atrophy of the skin.

Book Reviews

Biology of Acarus Scabiei. By Reuben Friedman, M.D. Price $3.00. Pp. 176, with 112 illustrations. New York: Froben Press, Inc., 1942.

The author, an authority on scabies, has published two previous books and contributes a most comprehensive account of the biology of Sarcoptes scabiei. The first chapter contains information about mites in general, and the second relates the story of the slow evolution of knowledge of scabies. The first part of the third and main chapter is devoted to minute anatomic descriptions of the male and female sarcoptes, nymphs, larvae and eggs; the second part deals with the biologic features of the organisms and includes detailed accounts of their habits.

Among the many curious facts about sarcoptes cited the following appears particularly interesting: The name *acarus*, from Greek ακαρί, which means uncuttable or indivisible, refers to the minute size of sarcoptes, which was long thought to represent the smallest possible living form and was therefore often called a "living atom" by sixteenth and seventeenth century writers. The inaccuracy of some of the early drawings of the parasite is astounding; probably the most fantastic representation of the itch mite is that published by Griendelius in 1687; the creature looks like a cross between a mouse and a grasshopper and could have been produced by Walt Disney. Mistakes and inadequacies in illustrations did not cease until the turn of the century. The redoubtable Linnaeus was already aware of the clinical significance of thyroglyphidae, for he correctly interpreted the eruption which appeared on the intertriginous surfaces of children dusted with meal powder as being caused by the flour mite contained in the meal.

One of the most remarkable biologic features of sarcoptes is the consistent choice of a site of predilection. For example, if female acari are confined to the forearm, they will burrow enough for concealment, but when the cell confining them is removed, they will leave these burrows and can be recovered on the wrist after periods varying from twenty minutes to two and a half hours. Another interesting feature is the influence of temperature on burrowing. Laboratory experiments have shown that female acari will not burrow if the temperature in the room is low; if, however, the experimentally infested hand is held over a radiator, the mites commence to burrow, and it is possible for one to regulate the rate of burrowing by alternately warming and cooling the hand.

Retrogressive movement of the acarus in her burrow is prevented by the dorsal spines. Larvae bore more deeply than adult organisms, and as a result of this deep boring exudation takes place in the form of vesicles which lie below the floor of the burrow and in its neighborhood. Thus not the adult organisms but the larvae cause the formation of vesicles, and the commonly held notion that the itch mite drowns itself in the serum produced as an inflammatory reaction against the invasion does not seem correct; it is more probable that the exudate provides food for the larva.

The photographic illustrations are excellent, and the reviewer knows of no other text on scabies in which their level of perfection is even approached. The book is printed on glazed paper in large clear type. The binding is substantial albeit rather somber in its unrelieved black.

This volume illustrates a fact often observed in scientific work: The most comprehensive and exact accounts are given by those workers who have concentrated the major part of their endeavors on the study of single, limited portions of their chosen fields. Future generations of dermatologists will rightly feel grateful to the author for his excellent contributions to the knowledge of scabies.

Notable Contributors to the Knowledge of Syphilis. By Herman Goodman, M.D. Price $3.00. Pp. 144, with 143 black and white illustrations. New York: Froben Press, Inc., 1943.

From the size of this little book one would not think it contains more references to writings on syphilis than any volume previously written. It is therefore a valuable work of reference. Again, one might not think that disjointed paragraphs, some of them consisting of only a few lines, could tell a consecutive and interesting story. However, such is the case, and the reader will be fascinated by the way the story unfolds from pre-Columbian times to the present, going through ages of mysticism and leading up to the present scientific knowledge of syphilis.

In his introduction, the author says that "No one fact, no one person has stood alone. Each contributor to knowledge required the aid and assistance of those preceding him or contemporary with him." Many of the names included are familiar to all syphilologists, though some will be entirely unknown. The names of the latter are included because they expressed opinions about syphilis. As Dr. Victor Robinson said in an interesting foreword: The book is small but it was necessary to ransack great libraries to write it.

A valuable feature of the book is the inclusion of one hundred and twenty-five portraits of contributors to the knowledge of syphilis. Those of more recent investigators are reproductions of actual photographs, whereas those of the earlier ones are mainly traditional, as the author states.

The author has been fair in citing authors who discussed the American origin of syphilis, a subject that has often given rise to acrimonious comments. He does not express any opinion himself regarding this question.

The volume is attractively printed on glazed paper. The small size of the book is not in proportion to its great value to all who are interested in the history of syphilis. It is an invaluable work, which reflects great credit on the unflagging industry of the author and his fairness in citing all who have contributed something to the history of syphilis.

Directory of Dermatologic Societies *

INTERNATIONAL

Tenth International Congress of Dermatology and Syphilology

Oliver S. Ormsby, President, 25 E. Washington St., Chicago.
Paul A. O'Leary, Secretary-General, 102-2d Ave. S. W., Rochester, Minn.
Place: New York. Time: Postponed indefinitely.

Pan American Medical Association, Section of Dermatology and Syphilology

J. J. Eller, President, 745–5th Ave., New York.
Austin W. Cheever, Secretary, 464 Beacon St., Boston.

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

B. Usher, President, 1538 Sherbrooke St. W., Montreal.
Frederick Kalz, Secretary-Treasurer, 1414 Drummond St., Montreal.

Royal Society of Medicine, Section of Dermatology

H. W. Barber, President, 7 Devonshire Pl., London, W. 1, England.
Louis Forman, Secretary, 7 Devonshire Pl., London, W. 1, England.

Sociedad Mexicana de Dermatología

Ernesto Escalona, President, Casa del Niño 79, Mexico, Mexico.
Fernando Latapi, Secretary, Zacatecas 220-6, Mexico, Mexico.

NATIONAL

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilolgy

Clark W. Finnerud, Chairman, 55 E. Washington St., Chicago.
Nelson P. Anderson, Secretary, 2007 Wilshire Blvd., Los Angeles.
Place: Chicago. Time: June 12-16, 1944.

American Academy of Dermatology and Syphilology

George M. MacKee, President, 999–5th Ave., New York.
Earl D. Osborne, Secretary, 471 Delaware Ave., Buffalo, N. Y.

American Board of Dermatology and Syphilology

Howard Fox, President, 140 E. 54th St., New York.
C. Guy Lane, Secretary-Treasurer, 416 Marlborough St., Boston.

American Dermatological Association

Joseph Klauder, President, 1934 Spruce St., Philadelphia.
Harry R. Foerster, Secretary, 208 E. Wisconsin Ave., Milwaukee.

Society for Investigative Dermatology

Fred D. Weidman, President, 1930 Chestnut St., Philadelphia.
S. William Becker, Secretary, 8 S. Michigan Ave., Chicago.

SECTIONAL

Central States Dermatological Association

John E. Rauschkolb, Secretary-Treasurer, 1808 Republic Bldg., Cleveland.
Place: Cleveland. Time: Postponed indefinitely.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

MISSISSIPPI VALLEY DERMATOLOGICAL SOCIETY

Lawrence C. Goldberg, Secretary-Treasurer, 623 Doctors Bldg., Cincinnati.
Place: Chicago.

NEW ENGLAND DERMATOLOGICAL SOCIETY

Jacob H. Swartz, President, 371 Commonwealth Ave., Boston.
Francis M. Thurmon, Secretary, 520 Commonwealth Ave., Boston.

NORTHERN NEW JERSEY DERMATOLOGICAL SOCIETY

John Kiley, President, 94 Park St., Montclair.
Henry Abel, Secretary, 339 Union Ave., Elizabeth.
Place: Academy of Medicine of Northern New Jersey, Newark. Time: Third Tuesday of March, April, October and December.

SOUTHEASTERN DERMATOLOGICAL ASSOCIATION

Howard Hailey, Chairman, 107 Doctors Bldg., Atlanta, Ga.
A. H. Lancaster, Secretary, P. O. Box 585, Knoxville, Tenn.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Dudley C. Smith, Chairman, University of Virginia Hospital, Charlottesville, Va.
J. Lamar Callaway, Secretary, Duke Hospital, Durham, N. C.

STATE

CALIFORNIA MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, DERMATOLOGY AND SYPHILOLOGY SECTION

Irving R. Bancroft, Chairman, 1052 W. 6th St., Los Angeles.
Chris Halloran, Secretary, 1052 W. 6th St., Los Angeles.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY

Harry Bailey, Chairman, 242 Trumbull St., Hartford.
Louis O'Brasky, Secretary, 1172 Chapel St., New Haven.

FLORIDA SOCIETY OF DERMATOLOGY AND SYPHILOLOGY

Wiley M. Sams, Chairman, 25 S. E. 2d Ave., Miami.
Lauren M. Sompayrac, Secretary, 117 W. Duval St., Jacksonville.

LOUISIANA DERMATOLOGICAL SOCIETY

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, 921 Canal St., New Orleans.

MASSACHUSETTS MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

John G. Downing, President, 520 Commonwealth Ave., Boston.
G. Marshall Crawford, Secretary, 1101 Beacon St., Boston.

MEDICAL SOCIETY OF THE STATE OF NEW YORK, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Harry C. Saunders, Chairman, 159 W. 87th St., New York.
James W. Jordan, Secretary, 471 Delaware Ave., Buffalo.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, SECTION ON DERMATOLOGY

Bernhard A. Goldmann, Chairman, 500 Penn Ave., Pittsburgh.
M. A. Pettler, Secretary, 1319–8th Ave., Beaver Falls.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

William G. Wander, Chairman, 504 Kales Bldg., Detroit.
Ruth Herrick, Secretary, 607 Medical Arts Bldg., Grand Rapids 2.

Minnesota Dermatological Society

S. E. Sweitzer, President, 825 Nicollet Ave., Minneapolis.
Harry A. Cumming, Secretary-Treasurer 419 Medical Arts Bldg., Minneapolis.
Time: First Friday in January, April, July and October.

Oklahoma State Dermatological Society

John H. Lamb Jr., President, Medical Arts Bldg., Oklahoma City.
M. M. Wickham, Secretary, 716 W. Symmes St., Norman.

Texas Dermatological Society

J. Lewis Pipkin, President, 705 E. Houston St., San Antonio.
Duncan O. Poth, Secretary-Treasurer, 414 Navarro St., San Antonio.

LOCAL

Baltimore-Washington Dermatological Society

H. Hanford Hopkins, Chairman, 1123 St. Paul St., Baltimore.
Reuben Goodman, Secretary-Treasurer, 1746 K St. N. W., Washington, D. C.
Place: Alternate cities. Time: Third Thursday of each month.

Bronx' Dermatological Society

David Bloom, President, 135 E. 50th St., New York.
Henry Silver, Secretary, 290 West End Ave., New York.
Time: Fourth Thursday of each month from October to May, inclusive.

Brooklyn Dermatological Society

T. Chiaramonte, President, 1 Nevins St., Brooklyn.
J. Schweig, Secretary, 47 E. 61st St., New York.
Time: Third Monday of each month except June, July, August and September.

Buffalo-Rochester Dermatological Society

James W. Jordon, President, 471 Delaware Ave., Buffalo.
Frank A. Dolce, Secretary-Treasurer, 468 Delaware Ave., Buffalo.

Central New York Dermatological Society

Albert Van Vranken, President, 1565 Union St., Schenectady.
Maxwell C. Snider, Secretary, 106 Oak St., Binghamton.

Chicago Dermatological Society

Michael H. Ebert, President, 25 E. Washington St., Chicago.
Marcus R. Caro, Secretary-Treasurer, 25 E. Washington St., Chicago.

Cincinnati Society of Dermatology and Syphilology

Harry L. Claasen, President, Provident Bank Bldg., Cincinnati.
Lawrence C. Goldberg, Secretary-Treasurer, 623 Doctors Bldg., Cincinnati.
Place: Cincinnati. Time: First Wednesday of each month, except July, August and September.

Cleveland Dermatological Society

J. R. Driver, President, 1422 Euclid Ave., Cleveland.
G. W. Binkley, Secretary, 10515 Carnegie Ave., Cleveland.
Time: Fourth Thursday of each month from September to May, inclusive.

Detroit Dermatological Society

Robert C. Jamieson, President, 1553 Woodward Ave., Detroit.
James R. Rogin, Secretary-Treasurer, 2306 Eaton Tower, Detroit.

Kansas City (Mo.) Dermatological Society

C. C. Dennie, President, 1103 Grand Ave., Kansas City.
Thomas B. Hall, Secretary, 902 Professional Bldg., Kansas City.

LOS ANGELES DERMATOLOGICAL SOCIETY

William H. Goeckerman, President, 727 W. 7th St., Los Angeles.
C. Russell Anderson, Secretary, 1930 Wilshire Blvd., Los Angeles.
Time: Second Tuesday of each month, October to May, inclusive.

MANHATTAN DERMATOLOGIC SOCIETY

Anthony C. Cipollaro, Chairman, 40 E. 61st St., New York.
Wilbert Sachs, Secretary, 57 W. 57th St., New York.

METROPOLITAN DERMATOLOGICAL SOCIETY

Laird Van Dyke, President, 206 E. 17th St., New York.
Royal M. Montgomery, Secretary, 57 W. 57th St., New York.

MONTREAL DERMATOLOGICAL SOCIETY

Paul Poirier, President, 456 Sherbrooke St. E., Montreal, Canada.
Alphonse Bernier, Secretary, 3995 St. Denis St., Montreal.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

David Bloom, Chairman, 135 E. 50th St., New York.
George M. Lewis, Secretary, 121 E. 60th St., New York.

NEW YORK DERMATOLOGICAL SOCIETY

Edward R. Maloney, President, 136 E. 64th St., New York.
J. Gardner Hopkins, Secretary-Treasurer, 630 W. 168th St., New York.

OMAHA DERMATOLOGICAL SOCIETY

Donald J. Wilson, President, 1113 Medical Arts Bldg., Omaha.
Leonard J. Owen, Secretary-Treasurer, 954 Stuart Bldg., Lincoln, Neb.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Carroll S. Wright, Chairman, 1402 Spruce St., Philadelphia.
Carmen C. Thomas, Secretary, 1930 Chestnut St., Philadelphia.
Time: Third Friday of September, November, January, March and May.

PITTSBURGH DERMATOLOGICAL SOCIETY

M. F. Pettler, President, 1319-8th Ave., Beaver Falls, Pa.
Frederick Amshel, Secretary, 3401 Fifth Ave., Pittsburgh.
Time: Third Thursday of every month except July and August.

ST. LOUIS DERMATOLOGICAL SOCIETY

Norman Tobias, President, Missouri Theatre Bldg., St. Louis.
Joseph Grindon Jr., Secretary-Treasurer, 323 Lister Bldg., St. Louis.
Place: Barnard Free Skin and Cancer Hospital. Time: 2 p. m., second Wednesday of each month.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

Arne E. Ingels, President, 490 Post St., San Francisco.
Ervin Epstein, Secretary-Treasurer, 1904 Franklin St., Oakland, Calif.
Time: Third Friday of February, April, September and November.

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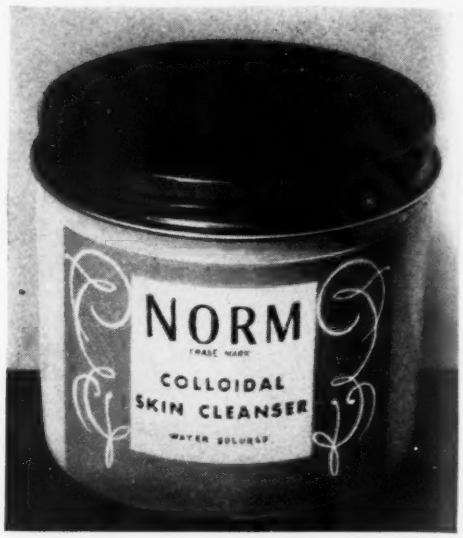

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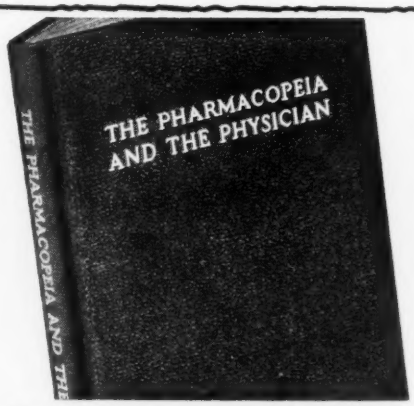

THE PHARMACOPEIA and THE PHYSICIAN

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